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(54) Title: A METHOD FOR EXTRACTING QUANTITATIVE INFORMATION RELATING TO AN INFLUENCE ON A CELLULAR RESPONSE

(57) **Abstract**

Cells are genetically modified to expresss a luminophore, e.g., a modified (F64L, S65T, Y66H) Green Fluorescent Protein (GFP, EGFP) coupled to a component of an intracellular signalling pathway such as a transcription factor, a cGMP– or cAMP–dependent protein kinase, a cyclin–, calmodulin– or phospholipid–dependent or mitogen–activated serine/threonin protein kinase, a tyrosine protein kinase, or a protein phosphatase (e.g. PKA, PKC, Erk, Smad, VASP, actin, p38, Jnk1, PKG, IkappaB, CDK2, Grk5, Zap70, p85, protein–tyrosine phosphatase 1C, Stat5, NFAT, NFkappaB, RhoA, PKB). An influence modulates the intracellular signalling pathway in such a way that the luminophore is being redistributed or translocated with the component in living cells in a manner experimentally determined to be correlated to the degree of the influence. Measurement of redistribution is performed by recording of light intensity, fluorescence lifetime, polarization, wavelength shift, resonance energy transfer, or other properties by an apparatus consisting of e.g. a fluorescence microscope and a CCD camera. Data stored as digital images are processed to numbers representing the degree of redistribution. The method can be used as a screening program for identifying a compound that modulates a component and is capable of treating a disease related to the function of the component.

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A METHOD for extracting quantitative information relating to an influence on a cellular response

FIELD OF INVENTION

The present invention relates to a method and tools for extracting quantitative information relating to an influence, on a cellular response, in particular an influence caused by contacting or incubating the cell with a substance influencing a cellular response, where the cellular response is manifested in redistribution of at least one component in the cell. In particular, the invention relates to a method for extracting quantitative information relating to an influence on an intracellular pathway involving redistribution of at least one component associated with the pathway. The method of the invention may be used as a very efficient procedure for testing or discovering the influence of a substance on a physiological process, for example in connection with screening for new drugs, testing of substances for toxicity, identifying drug targets for known or novel drugs. Other valuable uses of the method and technology of the invention will be apparent to the skilled person on the basis of the following disclosure. In a particular embodiment of the invention, the present invention relates to a method of detecting intracellular translocation or redistribution of biologically active polypeptides, preferably an enzyme, affecting intracellular processes, and a DNA construct and a cell for use in the method.

BACKGROUND OF THE INVENTION

Intracellular pathways are tightly regulated by a cascade of components that undergo modulation in a temporally and spatially characteristic manner. Several disease states can be attributed to altered activity of individual signalling components (i.e. protein kinases, protein phosphatases, transcription factors). These components therefore render themselves as attractive targets for therapeutic intervention.

Protein kinases and phosphatases are well described components of several intracellular signalling pathways. The catalytic activity of protein kinases and phosphatases are assumed to play a role in virtually all regulatable cellular processes. Although the involvement of protein kinases in cellular signalling and regulation have been subjected to extensive studies, detailed knowledge on e.g. the exact timing and spatial characteristics of signalling events is often difficult to obtain due to lack of a convenient technology.

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Novel ways of monitoring specific modulation of intracellular pathways in intact, living cells is assumed to provide new opportunities in drug discovery, functional genomics, toxicology, patient monitoring etc.

The spatial orchestration of protein kinase activity is likely to be essential for the high degree of specificity of individual protein kinases. The phosphorylation mediated by protein kinases is balanced by phosphatase activity. Also within the family of phosphatases translocation has been observed, e.g. translocation of PTP2C to membrane ruffles [(Cossette *et al.*1996)], and likewise is likely to be indicative of phosphatase activity.

Protein kinases often show a specific intracellular distribution before, during and after activation. Monitoring the translocation processes and/or redistribution of individual protein kinases or subunits thereof is thus likely to be indicative of their functional activity. A connection between translocation and catalytic activation has been shown for protein kinases like the diacyl glycerol (DAG)-dependent protein kinase C (PKC), the cAMP-dependent protein kinase (PKA) [(DeBernardi *et al.*1996)] and the mitogen-activated-protein kinase Erk-1 [(Sano *et al.*1995)].

Commonly used methods of detection of intracellular localisation/activity of protein kinases and phosphatases are immunoprecipitation, Western blotting and immunocytochemical detection.

Taking the family of diacyl glycerol (DAG)-dependent protein kinase Cs (PKCs) as an example, it has been shown that individual PKC isoforms that are distributed among different tissues and cells have different activator requirements and undergo differential translocation in response to activation. Catalytically inactive DAG-dependent PKCs are generally distributed throughout the cytoplasm, whereas they upon activation translocate to become associated with different cellular components, e.g. plasma membrane [(Farese, 1992),(Fulop Jr. *et al.*1995)] nucleus [(Khalil *et al.*1992)], cytoskeleton [(Blobe *et al.*1996)]. The translocation phenomenon being indicative of PKC activation has been monitored using different approaches: a) immunocytochemistry where the localisation of individual isoforms can be detected after permeabilisation and fixation of the cells [(Khalil *et al.*1992)]; and b) tagging all DAG-dependent PKC isoforms with a fluorescently labelled phorbol myristate acetate (PMA) [(Godson *et al.*1996)]; and c) chemical tagging PKC b1 with the fluorophore Cy3 [(Bastiaens & Jovin 1996)] and d) genetic tagging of PKCα ([Schmidt *et al.* 1997]) and of PKCγ and PKC ε ([Sakai *et al.* 1996]). The first method does not provide dynamic information whereas the latter methods will. Tagging PKC with fluorescently labelled phorbol myristate acetate cannot

distinguish between different DAG-dependent isoforms of PKC but will label and show movement of all isoforms. Chemical and genetic labelling of specific DAG-dependent PKCs confirmed that they in an isoform specific manner upon activation move to cell periphery or nucleus.

In an alternative method, protein kinase A activity has been measured in living cells by chemical labelling one of the kinase's subunit (Adams *et al.*1991). The basis of the methodology is that the regulatory and catalytic subunit of purified protein kinase A is labelled with fluorescein and rhodamine, respectively. At low cAMP levels protein kinase A is assembled in a heterotetrameric form which enables fluorescence resonance energy transfer between the two fluorescent dyes. Activation of protein kinase A leads to dissociation of the complex, thereby eliminating the energy transfer. A disadvantage of this technology is that the labelled protein kinase A has to be microinjected into the cells of interest. This highly invasive technique is cumbersome and not applicable to large scale screening of biologically active substances. A further disadvantage of this technique as compared to the presented invention is that the labelled protein kinase A cannot be inserted into organisms/animals as a transgene.

Recently it was discovered that Green Fluorescent Protein (GFP) expressed in many different cell types, including mammalian cells, became highly fluorescent [(Chalfie *et al.*1994)]. WO95/07463 describes a cell capable of expressing GFP and a method for detecting a protein of interest in a cell based on introducing into a cell a DNA molecule having DNA sequence encoding the protein of interest linked to DNA sequence encoding a GFP such that the protein produced by the DNA molecule will have the protein of interest fused to the GFP, then culturing the cells in conditions permitting expression of the fused protein and detecting the location of the fluorescence in the cell, thereby localizing the protein of interest in the cell. However, examples of such fused proteins are not provided, and the use of fusion proteins with GFP for detection or quantitation of translocation or redistribution of biologically active polypeptides affecting intracellular processes upon activation, such as proteins involved in signalling pathways, e.g. protein kinases or phosphatases, has not been suggested. WO 95/07463 further describes cells useful for the detection of molecules, such as hormones or heavy metals, in a biological sample, by operatively linking a regulatory element of the gene which is affected by the molecule of interest to a GFP, the presence of the molecules will affect the regulatory element which in turn will affect the expression of the GFP. In this way the gene encoding GFP is used as a reporter gene in a cell which is constructed for monitoring the presence of a specific molecular identity.

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Green Fluorescent Protein has been used in an assay for the detection of translocation of the glucocorticoid receptor (GR) [Carey, KL et al., The Journal of Cell Biology, Vol. 133, No. 5, p. 985-996 (1996)]. A GR-S65TGFP fusion has been used to study the mechanisms involved in translocation of the glucocorticoid receptor (GR) in response to the agonist dexamethasone from the cytosol, where it is present in the absence of a ligand, through the nuclear pore to the nucleus where it remains after ligand binding. The use of a GR-GFP fusion enables real-time imaging and quantitation of nuclear/cytoplasmic ratios of the fluorescence signal.

Many currently used screening programmes designed to find compounds that affect protein kinase activity are based on measurements of kinase phosphorylation of artificial or natural substrates, receptor binding and/or reporter gene expression.

DISCLOSURE OF THE INVENTION

The present invention provides an important new dimension in the investigation of cellular systems involving redistribution in that the invention provides quantification of the redistribution responses or events caused by an influence, typically contact with a chemical substance or mixture of chemical substances, but also changes in the physical environment. The quantification makes it possible to set up meaningful relationships, expressed numerically, or as curves or graphs, between the influences (or the degree of influences) on cellular systems and the redistribution response. This is highly advantageous because, as has been found, the quantification can be achieved in both a fast and reproducible manner, and - what is perhaps even more important - the systems which become quantifiable utilizing the method of the invention are systems from which enormous amounts of new information and insight can be derived.

The present screening assays have the distinct advantage over other screening assays, e.g., receptor binding assays, enzymatic assays, and reporter gene assays, in providing a system in which biologically active substances with completely novel modes of action, e.g. inhibition or promotion of redistribution/translocation of a biologically active polypeptide as a way of regulating its action rather than inhibition/activation of enzymatic activity, can be identified in a way that insures very high selectivity to the particular isoform of the biologically active polypeptide and further development of compound selectivity versus other isoforms of

the same biologically active polypeptide or other components of the same signalling pathway.

In its broadest aspect, the invention relates to a method for extracting quantitative information relating to an influence on a cellular response, the method comprising recording variation, caused by the influence on a mechanically intact living cell or mechanically intact living cells, in spatially distributed light emitted from a luminophore, the luminophore being present in the cell or cells and being capable of being redistributed in a manner which is related with the degree of the influence, and/or of being modulated by a component which is capable of being redistributed in a manner which is related to the degree of the influence, the association resulting in a modulation of the luminescence characteristics of the luminophore, detecting and recording the spatially distributed light from the luminophore, and processing the recorded variation in the spatially distributed light to provide quantitative information correlating the spatial distribution or change in the spatial distribution to the degree of the influence. In a preferred embodiment of the invention the luminophore, which is present in the cell or cells, is capable of being redistributed by modulation of an intracellular pathway, in a manner which is related to the redistribution of at least one component of the intracellular pathway. In another preferred embodiment of the invention, the luminophore is a fluorophore.

The cells

In the invention the cell and/or cells are mechanically intact and alive throughout the experiment. In another embodiment of the invention, the cell or cells is/are fixed at a point in time after the application of the influence at which the response has been predetermined to be significant, and the recording is made at an arbitrary later time.

The mechanically intact living cell or cells could be selected from the group consisting of fungal cell or cells, such as a yeast cell or cells; invertebrate cell or cells including insect cell or cells; and vertebrate cell or cells, such as mammalian cell or cells. This cell or these cells is/are incubated at a temperature of 30°C or above, preferably at a temperature of from 32°C to 39°C, more preferably at a temperature of from 35°C to 38°C, and most preferably at a temperature of about 37°C during the time period over which the influence is observed. In one aspect of the invention the mechanically intact living cell is part of a matrix of identical or non-identical cells.

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A cell used in the present invention should contain a nucleic acid construct encoding a fusion polypeptide as defined herein and be capable of expressing the sequence encoded by the construct. The cell is a eukaryotic cell selected from the group consisting of fungal cells, such as yeast cells; invertebrate cells including insect cells; vertebrate cells such as mammalian cells. The preferred cells are mammalian cells.

In another aspect of the invention the cells could be from an organism carrying in at least one of its component cells a nucleic acid sequence encoding a fusion polypeptide as defined herein and be capable of expressing said nucleic acid sequence. The organism is selected from the group consisting of unicellular and multicellular organisms, such as a mammal.

The luminophore

The luminophore is the component which allows the redistribution to be visualised and/or recorded by emitting light in a spatial distribution related to the degree of influence. In one embodiment of the invention, the luminophore is capable of being redistributed in a manner which is physiologically relevant to the degree of the influence. In another embodiment, the luminophore is capable of associating with a component which is capable of being redistributed in a manner which is physiologically relevant to the degree of the influence. In another embodiment, the luminophore correlation between the redistribution of the luminophore and the degree of the influence could be determined experimentally. In a preferred aspect of the invention, the luminophore is capable of being redistributed in substantially the same manner as the at least one component of an intracellular pathway. In yet another embodiment of the invention, the luminophore is capable of being quenched upon spatial association with a component which is redistributed by modulation of the pathway, the quenching being measured as a change in the intensity of the luminescence.

The luminophore could be a fluorophore. In a preferred embodiment of the invention, the luminophore could be a polypeptide encoded by and expressed from a nucleotide sequence harboured in the cell or cells. The luminophore could be a hybrid polypeptide comprising a fusion of at least a portion of each of two polypeptides one of which comprises a luminescent polypeptide and the other one of which comprises a biologically active polypeptide, as defined herein.

The luminescent polypeptide could be a GFP as defined herein or could be selected from the group consisting of green fluorescent proteins having the F64L mutation as defined herein

such as F64L-GFP, F64L-Y66H-GFP, F64L-S65T-GFP, and EGFP. The GFP could be N- or C-terminally tagged, optionally via a peptide linker, to the biologically active polypeptide or a part or a subunit thereof. The fluorescent probe could be a component of a intracellular signalling pathway. The probe is coded for by a nucleic acid construct.

The pathway of investigation in the present invention could be an intracellular signalling pathway.

The influence

In a preferred embodiment of the invention, the influence could be contact between the mechanically intact living cell or the group of mechanically intact living cells with a chemical substance and/or incubation of the mechanically intact living cell or the group of mechanically intact living cells with a chemical substance. The influence will modulate the intracellular processes. In one aspect the modulation could be an activation of the intracellular processes. In another aspect the modulation could be an deactivation of the intracellular processes. In yet another aspect, the influence could inhibit or promote the redistribution without directly affecting the metabolic activity of the component of the intracellular processes.

In one embodiment the invention is used as a basis for a screening program, where the effect of unknown influences such as a compound library, can be compared to influence of known reference compounds under standardised conditions.

The recording

In addition to the intensity, there are several parameters of fluorescence or luminescence which can be modulated by the effect of the influence on the underlying cellular phenomena, and can therefore be used in the invention. Some examples are resonance energy transfer, fluorescence lifetime, polarisation, wavelength shift. Each of these methods requires a particular kind of filter in the emission light path to select the component of the light desired and reject other components. The recording of property of light could be in the form of an ordered array of values such as a CCD array or a vacuum tube device such as a vidicon tube.

In one embodiment of the invention, the spatially distributed light emitted by a luminophore could be detected by a change in the resonance energy transfer between the luminophore and another luminescent entity capable of delivering energy to the luminophore, each of

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which has been selected or engineered to become part of, bound to or associated with particular components of the intracellular pathway. In this embodiment, either the luminophore or the luminescent entity capable of delivering energy to the luminophore undergoes redistribution in response to an influence. The resonance energy transfer would be measured as a change in the intensity of emission from the luminophore, preferably sensed by a single channel photodetector which responds only to the average intensity of the luminophore in a non-spatially resolved fashion.

In one embodiment of the invention, the recording of the spatially distributed light could be made at a single point in time after the application of the influence. In another embodiment, the recording could be made at two points in time, one point being before, and the other point being after the application of the influence. The result or variation is determined from the change in fluorescence compared to the fluorescence measured prior to the influence or modulation. In another embodiment of the invention, the recording could be performed at a series of points in time, in which the application of the influence occurs at some time after the first time point in the series of recordings, the recording being performed, e.g., with a predetermined time spacing of from 0.1 seconds to 1 hour, preferably from 1 to 60 seconds, more preferably from 1 to 30 seconds, in particular from 1 to 10 seconds, over a time span of from 1 second to 12 hours, such as from 10 seconds to 12 hours, e.g., from 10 seconds to one hour, such as from 60 seconds to 30 minutes or 20 minutes. The result or variation is determined from the change in fluorescence over time. The result or variation could also be determined as a change in the spatial distribution of the fluorescence over time.

Apparatus

The recording of spatially distributed luminescence emitted from the luminophore is performed by an apparatus for measuring the distribution of fluorescence in the cell or cells, and thereby any change in the distribution of fluorescence in the cell or cells, which includes at a minimum the following component parts: (a) a light source, (b) a method for selecting the wavelength(s) of light from the source which will excite the fluorescence of the protein, (c) a device which can rapidly block or pass the excitation light into the rest of the system, (d) a series of optical elements for conveying the excitation light to the specimen, collecting the emitted fluorescence in a spatially resolved fashion, and forming an image from this fluorescence emission, (e) a bench or stand which holds the container of the cells being measured in a predetermined geometry with respect to the series of optical elements, (f) a detector to

record the spatially resolved fluorescence in the form of an image, (g) a computer or electronic system and associated software to acquire and store the recorded images, and to compute the degree of redistribution from the recorded images.

In a preferred embodiment of the invention the apparatus system is automated. In one embodiment the components in d and e mentioned above comprise a fluorescence microscope. In one embodiment the component in f mentioned above is a CCD camera.

In one embodiment the image is formed and recorded by an optical scanning system.

In one embodiment a liquid addition system is used to add a known or unknown compound to any or all of the cells in the cell holder at a time determined in advance. Preferably, the liquid addition system is under the control of the computer or electronic system. Such an automated system can be used for a screening program due to its ability to generate results from a larger number of test compounds than a human operator could generate using the apparatus in a manual fashion.

Quantitation of the influence

The recording of the variation or result with respect to light emitted from the luminophore is performed by recording the spatially distributed light as one or more digital images, and the processing of the recorded variation to reduce it to one or more numbers representative of the degree of redistribution comprises a digital image processing procedure or combination of digital image processing procedures. The quantitative information which is indicative of the degree of the cellular response to the influence or the result of the influence on the intracellular pathway is extracted from the recording or recordings according to a predetermined calibration based on responses or results, recorded in the same manner, to known degrees of a relevant specific influence. This calibration procedure is developed according to principles described below (Developing an Image-based Assay Technique). Specific descriptions of the procedures for particular assays are given in the examples.

While the stepwise procedure necessary to reduce the image or images to the value representative of the is particular to each assay, the individual steps are generally well-known methods of image processing. Some examples of the individual steps are point operations such as subtraction, ratioing, and thresholding, digital filtering methods such as smoothing, sharpening, and edge detection, spatial frequency methods such as Fourier filtering, image cross-correlation and image autocorrelation, object finding and classification (blob analysis),

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and colour space manipulations for visualisation. In addition to the algorithmic procedures, heuristic methods such as neural networks may also be used.

Nucleic acid constructs

The nucleic acid constructs used in the present invention encode in their nucleic acid sequences fusion polypeptides comprising a biologically active polypeptide that is a component of an intracellular signalling pathway, or a part thereof, and a GFP, preferably an F64L mutant of GFP, N- or C-terminally fused, optionally via a peptide linker, to the biologically active polypeptide or part thereof.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a protein kinase or a phosphatase.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a transcription factor or a part thereof which changes cellular localisation upon activation.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a protein, or a part thereof, which is associated with the cytoskeletal network and which changes cellular localisation upon activation.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a protein kinase or a part thereof which changes cellular localisation upon activation.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a serine/threonine protein kinase or a part thereof capable of changing intracellular localisation upon activation.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a tyrosine protein kinase or a part thereof capable of changing intracellular localisation upon activation.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a phospholipid-dependent serine/threonine protein kinase or a part thereof capable of changing intracellular localisation upon activation.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a cAMP-dependent protein kinase or a part thereof capable of changing cellular localisation upon activation. In a preferred embodiment the biologically active polypeptide encoded by the nucleic acid construct is a PKAc-F64L-S65T-GFP fusion.

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In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a cGMP-dependent protein kinase or a part thereof capable of changing cellular localisation upon activation.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a calmodulin-dependent serine/threonine protein kinase or a part thereof capable of changing cellular localisation upon activation.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a mitogen-activated serine/threonine protein kinase or a part thereof capable of changing cellular localisation upon activation. In preferred embodiments the biologically active polypeptide encoded by the nucleic acid constructs are an ERK1-F64L-S65T-GFP fusion or an EGFP-ERK1 fusion.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a cyclin-dependent serine/threonine protein kinase or a part thereof capable of changing cellular localisation upon activation.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct is a protein phosphatase or a part thereof capable of changing cellular localisation upon activation.

In one preferred embodiment of the invention the nucleic acid constructs may be DNA constructs.

In one embodiment the biologically active polypeptide encoded by the nucleic acid construct In one embodiment the gene encoding GFP in the nucleic acid construct is derived from Aequorea victoria. In a preferred embodiment the gene encoding GFP in the nucleic acid construct is EGFP or a GFP variant selected from F64L-GFP, F64L-Y66H-GFP and F64L-S65T-GFP.

In preferred embodiments of the invention the DNA constructs which can be identified by any of the DNA sequences shown in SEQ ID NO: 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142 or are variants of these sequences capable of encoding the same fusion polypeptide or a fusion polypeptide which is biologically equivalent thereto, e.g. an isoform, or a splice variant or a homologue from another species.

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Screening program

The present invention describes a method that may be used to establish a screening program for the identification of biologically active substances that directly or indirectly affects intracellular signalling pathways and because of this property are potentially useful as medicaments. Based on measurements in living cells of the redistribution of spatially resolved luminescence from luminophores which undergo a change in distribution upon activation or deactivation of an intracellular signalling pathway the result of the individual measurement of each substance being screened indicates its potential biological activity.

In one embodiment of the invention the screening program is used for the identification of a biologically toxic substance as defined herein that exerts its toxic effect by interfering with an intracellular signalling pathway. Based on measurements in living cells of the redistribution of spatially resolved luminescence from luminophores which undergo a change in distribution upon activation or deactivation of an intracellular signalling pathway the result of the individual measurement of each substance being screened indicates its potential biologically toxic activity. In one embodiment of a screening program a compound that modulates a component of an intracellular pathway as defined herein, can be found and the therapeutic amount of the compound estimated by a method according to the method of the invention. In a preferred embodiment the present invention leads to the discovery of a new way of treating a condition or disease related to the intracellular function of a biologically active polypeptide comprising administration to a patient suffering from said condition or disease of an effective amount of a compound which has been discovered by any method according to the invention. In another preferred embodiment of the invention a method is established for identification of a new drug target or several new drug targets among the group of biologically active polypeptides which are components of intracellular signalling pathways.

In another embodiment of the invention an individual treatment regimen is established for the selective treatment of a selected patient suffering from an ailment where the available medicaments used for treatment of the ailment are tested on a relevant primary cell or cells obtained from said patient from one or several tissues, using a method comprising transfecting the cell or cells with at least one DNA sequence encoding a fluorescent probe according to the invention, transferring the transfected cell or cells back the said patient, or culturing the cell or cells under conditions permitting the expression of said probes and exposing it to an array of the available medicaments, then comparing changes in fluorescence patterns or redistribution patterns of the fluorescent probes in the intact living cell or cells to

detect the cellular response to the specific medicaments (obtaining a cellular action profile), then selecting one or more medicament or medicaments based on the desired activity and acceptable level of side effects and administering an effective amount of these medicaments to the selected patient.

Back-tracking of a signal transduction pathway

The present invention describes a method that may be used to establish a screening program for back-tracking signal transduction pathways as defined herein. In one embodiment the screening program is used to establish more precisely at which level one or several compounds affect a specific signal transduction pathway by successively or in parallel testing the influence of the compound or compounds on the redistribution of spatially resolved luminescence from several of the luminophores which undergo a change in distribution upon activation or deactivation of the intracellular signalling pathway under study.

Construction and testing of probes

In general, a probe, i.e. a "GeneX"-GFP fusion or a GFP-"GeneX" fusion, is constructed using PCR with "GeneX"-specific primers followed by a cloning step to fuse "GeneX" in frame with GFP. The fusion may contain a short vector derived sequence between "GeneX" and GFP (e.g. part of a multiple cloning site region in the plasmid) resulting in a peptide linker between "GeneX" and GFP in the resulting fusion protein.

Detailed stepwise procedure:

- Identifying the sequence of the gene. This is most readily done by searching a depository of genetic information, e.g. the GenBank Sequence Database, which is widely available and routinely used by molecular biologists. In the specific examples below the GenBank Accession number of the gene in question is provided.

- Design of gene-specific primers. Inspection of the sequence of the gene allows design of gene-specific primers to be used in a PCR reaction. Typically, the top-strand primer encompasses the ATG start codon of the gene and the following ca. 20 nucleotides, while the bottom-strand primer encompasses the stop codon and the ca. 20 preceding nucleotides, if

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the gene is to be fused behind GFP, i.e. a GFP-"GeneX" fusion. If the gene is to be fused in front of GFP, i.e. a "GeneX"-GFP fusion, a stop codon must be avoided. Optionally, the full length sequence of GeneX may not be used in the fusion, but merely the part which localizes and redistributes like GeneX in response to a signal.

In addition to gene-specific sequences, the primers contain at least one recognition sequence for a restriction enzyme, to allow subsequent cloning of the PCR product. The sites are chosen so that they are unique in the PCR product and compatible with sites in the cloning vector. Furthermore, it may be necessary to include an exact number of nucleotides between the restriction enzyme site and the gene-specific sequence in order to establish the correct reading frame of the fusion gene and/or a translation initiation consensus sequence. Lastly, the primers always contain a few nucleotides in front of the restriction enzyme site to allow efficient digestion with the enzyme.

-Identifying a source of the gene to be amplified. In order for a PCR reaction to produce a product with gene-specific primers, the gene-sequence must initially be present in the reaction, e.g. in the form of cDNA. Information in GenBank or the scientific literature will usually indicate in which tissue(s) the gene is expressed, and cDNA libraries from a great variety of tissues or cell types from various species are commercially available, e.g. from Clontech (Palo Alto), Stratagene (La Jolla) and Invitrogen (San Diego). Many genes are also available in cloned form from The American Type Tissue Collection (Virginia).

- Optimizing the PCR reaction. Several factors are known to influence the efficiency and specificity of a PCR reaction, including the annealing temperature of the primers, the concentration of ions, notably Mg^{2+} and K^{+}, present in the reaction, as well as pH of the reaction. If the result of a PCR reaction is deemed unsatisfactory, it might be because the parameters mentioned above are not optimal. Various annealing temperatures should be tested, e.g. in a PCR machine with a built-in temperature gradient, available from e.g. Stratagene (La Jolla), and/or various buffer compositions should be tried, e.g. the OptiPrime buffer system from Stratagene (La Jolla).

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- Cloning the PCR product. The vector into which the amplified gene product will be cloned and fused with GFP will already have been taken into consideration when the primers were designed. When choosing a vector, one should at least consider in which cell types the probe subsequently will be expressed, so that the promoter controlling expression of the probe is compatible with the cells. Most expression vectors also contain one or more selective markers, e.g. conferring resistance to a drug, which is a useful feature when one wants to make stable transfectants. The selective marker should also be compatible with the cells to be used.

The actual cloning of the PCR product should present no difficulty as it typically will be a one-step cloning of a fragment digested with two different restriction enzymes into a vector digested with the same two enzymes. If the cloning proves to be problematic, it may be because the restriction enzymes did not work well with the PCR fragment. In this case one could add longer extensions to the end of the primers to overcome a possible difficulty of digestion close to a fragment end, or one could introduce an intermediate cloning step not based on restriction enzyme digestion. Several companies offer systems for this approach, e.g. Invitrogen (San Diego) and Clontech (Palo Alto).

Once the gene has been cloned and, in the process, fused with the GFP gene, the resulting product, usually a plasmid, should be carefully checked to make sure it is as expected. The most exact test would be to obtain the nucleotide sequence of the fusion-gene.

Testing the probe

Once a DNA construct for a probe has been generated, its functionality and usefulness may be tested by subjecting it to the following tests:

- Transfecting it into cells capable of expressing the probe. The fluorescence of the cell is inspected soon after, typically the next day. At this point, two features of cellular fluorescence are noted: the intensity and the sub-cellular localization.

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The intensity should usually be at least as strong as that of unfused GFP in the cells. If it is not, the sequence or quality of the probe-DNA might be faulty, and should be carefully checked.

The sub-cellular localization is an indication of whether the probe is likely to perform well. If it localizes as expected for the gene in question, e.g. is excluded from the nucleus, it can immediately go on to a functional test. If the probe is not localized soon after the transfection procedure, it may be because of overexpression at this point in time, as the cell typically will have taken of very many copies of the plasmid, and localization will occur in time, e.g. within a few weeks, as plasmid copy number and expression level decreases. If localization does not occur after prolonged time, it may be because the fusion to GFP has destroyed a localization function, e.g. masked a protein sequence essential for interaction with its normal cellular anchor-protein. In this case the opposite fusion might work, e.g. if GeneX-GFP does not work, GFP-GeneX might, as two different parts of GeneX will be affected by the proximity to GFP. If this does not work, the proximity of GFP at either end might be a problem, and it could be attempted to increase the distance by incorporating a longer linker between GeneX and GFP in the DNA construct.

If there is no prior knowledge of localization, and no localization is observed, it may be because the probe should not be localized at this point, because such is the nature of the protein fused to GFP. It should then be subjected to a functional test.

In a functional test, the cells expressing the probe are treated with at least one compound known to perturb, usually by activating, the signalling pathway on which the probe is expected to report by redistributing itself within the cell. If the redistribution is as expected, e.g. if prior knowledge tell that it should translocate from location X to location Y, it has passed the first critical test. In this case it can go on to further characterization and quantification of the response.

If it does not perform as expected, it may be because the cell lacks at least one component of the signalling pathway, e.g. a cell surface receptor, or there is species incompatibility, e.g. if the probe is modelled on sequence information of a human geneproduct, and the cell is of hamster origin. In both instances one should identify other cell types for the testing process where these potential problems would not apply.

If there is no prior knowledge about the pattern of redistribution, the analysis of the redistribution will have to be done in greater depth to identify what the essential and indicative features are, and when this is clear, it can go on to further characterization and quantification of the response. If no feature of redistribution can be identified, the problem might be as mentioned above, and the probe should be retested under more optimal cellular conditions.

If the probe does not perform under optimal cellular conditions it's back to the drawing board.

Developing an image-based assay technique

The process of developing an image-based redistribution assay begins with either the unplanned experimental observation that a redistribution phenomenon can be visualised, or the design of a probe specifically to follow a redistribution phenomenon already known to occur. In either event, the first and best exploratory technique is for a trained scientist or technician to observe the phenomenon. Even with the rapid advances in computing technology, the human eye-brain combination is still the most powerful pattern recognition system known, and requires no advance knowledge of the system in order to detect potentially interesting and useful patterns in raw data. This is especially if those data are presented in the form of images, which are the natural "data type" for human visual processing. Because human visual processing operates most effectively in a relatively narrow frequency range, i.e., we cannot see either very fast or very slow changes in our visual field, it may be necessary to record the data and play it back with either time dilation or time compression.

Some luminescence phenomena cannot be seen directly by the human eye. Examples include polarization and fluorescence lifetime. However, with suitable filters or detectors, these signals can be recorded as images or sequences of images and displayed to the human in the fashion just described. In this way, patterns can be detected and the same methods can be applied.

Once the redistribition has been determined to be a reproducible phenomenon, one or more data sets are generated for the purpose of developing a procedure for extracting the quantitative information from the data. In parallel, the biological and optical conditions are determined which will give the best quality raw data for the assay. This can become an iterative process; it may be necessary to develop a quantitative procedure in order to assess the effect on the assay of manipulating the assay conditions.

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The data sets are examined by a person or persons with knowledge of the biological phenomenon and skill in the application of image processing techniques. The goal of this exercise is to determine or at least propose a method which will reduce the image or sequence of images constituting the record of a "response" to a value corresponding to the degree of the response. Using either interactive image processing software or an image processing toolbox and a programming language, the method is encoded as a procedure or algorithm which takes the image or images as input and generates the degree of response (in any units) as its output. Some of the criteria for evaluating the validity of a particular procedure are:

- Does the degree of the response vary in a biologically significant fashion, i.e., does it show the known or putative dependence on the concentration of the stimulating agent or condition?
- Is the degree of response reproducible, i.e., does the same concentration or level of stimulating agent or condition give the same response with an acceptable variance?
- Is the dynamic range of the response sufficient for the purpose of the assay? If not, can a change in the procedure or one of its parameters improve the dynamic range?
- Does the procedure exhibit any clear "pathologies", i.e., does it give ridiculous values for the response if there are commonly occurring imperfections in the imaging process? Can these pathologies be eliminated, controlled, or accounted for?
- Can the procedure deal with the normal variation in the number and/or size of cells in an image?

In some cases the method may be obvious; in others, a number of possible procedures may suggest themselves. Even if one method appears clearly superior to others, optimisation of parameters may be required. The various procedures are applied to the data set and the criteria suggested above are determined, or the single procedure is applied repeatedly with adjustment of the parameter or parameters until the most satisfactory combination of signal, noise, range, etc. are arrived at. This is equivalent to the calibration of any type of single-channel sensor.

The number of ways of extracting a single value from an image are extremely large, and thus an intelligent approach must be taken to the initial step of reducing this number to a small, finite number of possible procedures. This is not to say that the procedure arrived at is

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necessarily the best procedure - but a global search for the best procedure is simply out of the question due to the sheer number of possibilities involved.

Image-based assays are no different than other assay techniques in that their usefulness is characterised by parameters such as the specificity for the desired component of the sample, the dynamic range, the variance, the sensitivity, the concentration range over which the assay will work, and other such parameters. While it is not necessary to characterise each and every one of these before using the assay, they represent the only way to compare one assay with another.

Example: Developing a Quantitative assay for GLUT4 Translocation

GLUT4 is a member of the class of glucose transporter molecules which are important in cellular glucose uptake. It is known to translocate to the plasma membrane under some conditions of stimulation of glucose uptake. The ability to visualize the glucose uptake response noninvasively, without actually measuring glucose uptake, would be a very useful assay for anyone looking for, for example, treatments for type II diabetes.

A CHO cell line which stably expressed the human insulin receptor was used as the basis for a new cell line which stably expressed a fusion between GLUT4 and GFP. This cell line was expected to show translocation of GLUT4 to the plasma membrane as visualized by the movement of the GFP. The translocation could definitely be seen in the form of the appearance of local increases in the fluorescence in regions of the plasma membrane which had a characteristic shape or pattern. This is shown in Figure 12.

These objects became known as "snircles", and the phenomenon of their appearance as "snircling". In order to quantitate their appearance, a method had to be found to isolate them as objects in the image field, and then enumerate them, measure their area, or determine some parameter about them which correlated in a dose-dependent fashion with the concentration of insulin to which the cells had been exposed. In order to separate the snircles, a binarization procedure was applied in which one copy of the image smoothed with a relatively severe gaussian kernel (sigma = 2.5) was subtracted from another copy to which only a relatively light gaussian smooth had been applied (sigma=0.5). The resultant image was rescaled to its min/max range, and an automatic threshold was applied to divide the image into two levels. The thresholded image contains a background of one value all found object with another value. The found objects were first filtered through a filter to remove objects far too

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large and far too small to be snircles. The remaining objects, which represent snircles and other artifacts from the image with approximately the same size and intensity characteristics as snircles, are passed into a classification procedure which has been previously trained with many images of snircles to recognize snircles and exclude the other artifacts. The result of this procedure is a binary image which shows only the found snircles to the degree to which the classification procedure can accurately identify them. The total area of the snircles is then summed and this value is the quantitative measure of the degree of snircling for that image.

Definitions:

In the present specification and claims, the term "an influence" covers any influence to which the cellular response comprises a redistribution. Thus, e.g., heating, cooling, high pressure, low pressure, humidifying, or drying are influences on the cellular response on which the resulting redistribution can be quantified, but as mentioned above, perhaps the most important influences are the influences of contacting or incubating the cell or cells with substances which are known or suspected to exert and influence on the cellular response involving a redistribution contribution. In another embodiment of the invention the influence could be substances from a compound drug library.

In the present context, the term "green fluorescent protein" is intended to indicate a protein which, when expressed by a cell, emits fluorescence upon exposure to light of the correct excitation wavelength (cf. [(Chalfie *et al.*1994)]). In the following, GFP in which one or more amino acids have been substituted, inserted or deleted is most often termed "modified GFP". "GFP" as used herein includes wild-type GFP derived from the jelly fish *Aequorea victoria* and modifications of GFP, such as the blue fluorescent variant of GFP disclosed by Heim et al. (1994). Proc.Natl.Acad.Sci. 91:12501, and other modifications that change the spectral properties of the GFP fluorescence, or modifications that exhibit increased fluorescence when expressed in cells at a temperature above about 30°C described in PCT/DK96/00051, published as WO 97/11094 on 27 March 1997 and hereby incorporated by reference, and which comprises a fluorescent protein derived from *Aequorea* Green Fluorescent Protein (GFP) or any functional analogue thereof, wherein the amino acid in position 1 upstream from the chromophore has been mutated to provide an increase of fluorescence intensity when the

fluorescent protein of the invention is expressed in cells. Preferred GFP variants are F64L-GFP, F64L-Y66H-GFP and F64L-S65T-GFP. An especially preferred variant of GFP for use in all the aspects of this invention is EGFP (DNA encoding EGFP which is a F64L-S65T variant with codons optimized for expression in mammalian cells is available from Clontech, Palo Alto, plasmids containing the EGFP DNA sequence, cf. GenBank Acc. Nos. U55762, U55763).

The term "intracellular signalling pathway" and "signal transduction pathway" are intended to indicate the coordinated intracellular processes whereby a living cell transduce an external or internal signal into cellular responses. Said signal transduction will involve an enzymatic reaction said enzymes include but are not limited to protein kinases, GTPases, ATPases, protein phosphatases, phospholipases. The cellular responses include but are not limited to gene transcription, secretion, proliferation, mechanical activity, metabolic activity, cell death.

The term "second messenger" is used to indicate a low molecular weight component involved in the early events of intracellular signal transduction pathways.

The term "luminophore" is used to indicate a chemical substance which has the property of emitting light either inherently or upon stimulation with chemical or physical means. This includes but is not limited to fluorescence, bioluminescence, phosphorescence, chemiluminescence.

The term "mechanically intact living cell" is used to indicate a cell which is considered living according to standard criteria for that particular type of cell such as maintenance of normal membrane potential, energy metabolism, proliferative capability, and has not experienced any physically invasive treatment designed to introduce external substances into the cell such as microinjection.

The term "physiologically relevant" ,when applied to an experimentally determined redistribution of an intracellular component, as measured by a change in the luminescence properties or distribution, is used to indicate that said redistribution can be explained in terms of the underlying biological phenomenon which gives rise to the redistribution.

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Th terms "image processing" and "image analysis" are used to describe a large family of digital data analysis techniques or combination of such techniques which reduce ordered arrays of numbers (images) to quantitative information describing those ordered arrays of numbers. When said ordered arrays of numbers represent measured values from a physical process, the quantitative information derived is therefore a measure of the physical process.

The term "fluorescent probe" is used to indicate a fluorescent fusion polypeptide comprising a GFP or any functional part thereof which is N- or C-terminally fused to a biologically active polypeptide as defined herein, optionally via a peptide linker consisting of one or more amino acid residues, where the size of the linker peptide in itself is not critical as long as the desired functionality of the fluorescent probe is maintained. A fluorescent probe according to the invention is expressed in a cell and basically mimics the physiological behaviour of the biologically active polypeptide moiety of the fusion polypeptide.

The term "mammalian cell" is intended to indicate any living cell of mammalian origin. The cell may be an established cell line, many of which are available from The American Type Culture Collection (ATCC, Virginia, USA) or a primary cell with a limited life span derived from a mammalian tissue, including tissues derived from a transgenic animal, or a newly established immortal cell line derived froma mammalian tissue including transgenic tissues, or a hybrid cell or cell line derived by fusing different celltypes of mammalian origin e.g. hybridoma cell lines. The cells may optionally express one or more non-native gene products, e.g. receptors, enzymes, enzyme substrates, prior to or in addition to the fluorescent probe. Preferred cell lines include but are not limited to those of fibroblast origin, e.g. BHK, CHO, BALB, or of endothelial origin, e.g. HUVEC, BAE (bovine artery endothelial), CPAE (cow pulmonary artery endothelial) or of pancreatic origin, e.g. RIN, INS-1, MIN6, bTC3, aTC6, bTC6, HIT, or of hematopoietic origin, e.g. adipocyte origin, e.g. 3T3-L1, neuronal/neuroendocrine origin, e.g. AtT20, PC12, GH3, muscle origin, e.g. SKMC, A10, C2C12, renal origin, e.g. HEK 293, LLC-PK1.

The term "hybrid polypeptide" is intended to indicate a polypeptide which is a fusion of at least a portion of each of two proteins, in this case at least a portion of the green fluorescent protein, and at least a portion of a catalytic and/or regulatory domain of a protein kinase. Furthermore a hybrid polypeptide is intended to indicate a fusion polypeptide comprising a

GFP or at least a portion of the green fluorescent protein that contains a functional fluorophore, and at least a portion of a biologically active polypeptide as defined herein provided that said fusion is not the PKCα-GFP, PKCγ-GFP, and PKCε-GFP disclosed by Schmidt et al.and Sakai et al., respectively. Thus, GFP may be N- or C-terminally tagged to a biologically active polypeptide, optionally via a linker portion or linker peptide consisting of a sequence of one or more amino acids. The hybrid polypeptide or fusion polypeptide may act as a fluorescent probe in intact living cells carrying a DNA sequence encoding the hybrid polypeptide under conditions permitting expression of said hybrid polypeptide.

The term "kinase" is intended to indicate an enzyme that is capable of phosphorylating a cellular component.

The term "protein kinase" is intended to indicate an enzyme that is capable of phosphorylating serine and/or threonine and/or tyrosine in peptides and/or proteins.

The term "phosphatase" is intended to indicate an enzyme that is capable of dephosphorylating phosphoserine and/or phosphothreonine and/or phosphotyrosine in peptides and/or proteins.

In the present context, the term "biologically active polypeptide" is intended to indicate a polypeptide affecting intracellular processes upon activation, such as an enzyme which is active in intracellular processes or a portion thereof comprising a desired amino acid sequence which has a biological function or exerts a biological effect in a cellular system. In the polypeptide one or several aminoacids may have been deleted, inserted or replaced to alter its biological function, e.g. by rendering a catalytic site inactive. Preferably, the biologically active polypeptide is selected from the group consisting of proteins taking part in an intracellular signalling pathway, such as enzymes involved in the intracellular phosphorylation and dephosphorylation processes including kinases, protein kinases and phosphorylases as defined herein, but also proteins making up the cytoskeleton play important roles in intracellular signal transduction and are therefore included in the meaning of "biologically active polypeptide" herein. More preferably, the biologically active polypeptide is a protein which according to its state as activated or non-activated changes localisation within the cell, preferably as an in-

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termediary component in a signal transduction pathway. Included in this preferred group of biologically active polypeptides are cAMP dependent protein kinase A.

The term "a substance having biological activity" is intended to indicate any sample which has a biological function or exerts a biological effect in a cellular system. The sample may be a sample of a biological material such as a sample of a body fluid including blood, plasma, saliva, milk, urine, or a microbial or plant extract, an environmental sample containing pollutants including heavy metals or toxins, or it may be a sample containing a compound or mixture of compounds prepared by organic synthesis or genetic techniques.

The phrase "any change in fluorescence" means any change in absorption properties, such as wavelength and intensity, or any change in spectral properties of the emitted light, such as a change of wavelength, fluorescence lifetime, intensity or polarisation, or any change in the intracellular localisation of the fluorophore. It may thus be localised to a specific cellular component (e.g. organelle, membrane, cytoskeleton, molecular structure) or it may be evenly distributed throughout the cell or parts of the cell.

The phrase "back-tracking of a signal transduction pathway" is intended to indicate.

The term "organism" as used herein indicates any unicellular or multicellular organism preferably originating from the animal kingdom including protozoans, but also organisms that are members of the plant kingdoms, such as algae, fungi, bryophytes, and vascular plants are included in this definition.

The term "nucleic acid" is intended to indicate any type of poly- or oligonucleic acid sequence, such as a DNA sequence, a cDNA sequence, or an RNA sequence.

The term "biologically equivalent" as it relates to proteins is intended to mean that a first protein is equivalent to a second protein if the cellular functions of the two proteins may substitute for each other, e.g. if the two proteins are closely related isoforms encoded by different genes, if they are splicing variants, or allelic variants derived from the same gene, if they perform identical cellular functions in different cell types, or in different species. The term "biologically equivalent" as it relates to DNA is intended to mean that a first DNA sequ-

ence encoding a polypeptide is equivalent to a second DNA sequence encoding a polypeptide if the functional proteins encoded by the two genes are biologically equivalent.

The phrase "back-tracking of a signal transduction pathway" is intended to indicate a process for defining more precisely at what level a signal transduction pathway is affected, either by the influence of chemical compounds or a disease state in an organism. Consider a specific signal transduction pathway represented by the bioactive polypeptides A - B - C - D, with signal transduction from A towards D. When investigating all components of this signal transduction pathway compounds or disease states that influence the activity or redistribution of only D can be considered to act on C or downstream of C whereas compounds or disease states that influence the activity or redistribution of C and D, but not of A and B can be considered to act downstream of B.

The term "fixed cells" is used to mean cells treated with a cytological fixative such as glutaraldehyde or formaldehyde, treatments which serve to chemically cross-link and stabilize soluble and insoluble proteins within the structure of the cell. Once in this state, such proteins cannot be lost from the structure of the now-dead cell.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1. CHO cells expressing the PKAc-F64L-S65T-GFP hybrid protein have been treated in HAM's F12 medium with 50 mM forskolin at 37°C. The images of the GFP fluorescence in these cells have been taken at different time intervals after treatment, which were: a) 40 seconds b) 60 seconds c) 70 seconds d) 80 seconds. The fluorescence changes from a punctate to a more even distribution within the (non-nuclear) cytoplasm.

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Figure 2. Time-lapse analysis of forskolin induced PKAc-F64L-S65T-GFP redistribution. CHO cells, expressing the PKAc-F64L-S65T-GFP fusion protein were analysed by time-lapse fluorescence microscopy. Fluorescence micrographs were acquired at regular intervals from 2 min before to 8 min after the addition of agonist. The cells were challenged with 1 mM forskolin immediately after the upper left image was acquired (t=0). Frames were collected at the following times: i) 0, ii) 1, iii) 2, iv) 3, v) 4 and vi) 5 minutes. Scale bar 10 mm.

Figure 3. Time-lapse analyses of PKAc-F64L-S65T-GFP redistribution in response to various agonists. The effects of 1 mM forskolin (A), 50 mM forskolin (B), 1mM dbcAMP (C) and 100 mM IBMX (D) (additions indicated by open arrows) on the localisation of the PKAc-F64L-S65T-GFP fusion protein were analysed by time-lapse fluorescence microscopy of CHO/PKAc-F64L-S65T-GFP cells. The effect of addition of 10 mM forskolin (open arrow), followed shortly by repeated washing with buffer (solid arrow), on the localisation of the PKAc-F64L-S65T-GFP fusion protein was analysed in the same cells (E). In a parallel experiment, the effect of adding 10 mM forskolin and 100 mM IBMX (open arrow) followed by repeated washing with buffer containing 100 mM IBMX (solid arrow) was analysed (F). Removing forskolin caused PKAc-F64L-S65T-GFP fusion protein to return to the cytoplasmic aggregates while this is prevented by the continued presence of IBMX (F). The effect of 100 nM glucagon (Fig 3G, open arrow) on the localisation of the PKAc-F64L-S65T-GFP fusion protein is also shown for BHK/GR, PKAc-F64L-S65T-GFP cells. The effect of 10 mM norepinephrine (H), solid arrow, on the localisation of the PKAc-F64L-S65T-GFP fusion protein was analysed similarly, in transiently transfected CHO, PKAc-F64L-S65T-GFP cells, pretreated with 10 mM forskolin, open arrow, to increase $[cAMP]_i$. N.B. in Fig 3H the x-axis counts the image numbers, with 12 seconds between images. The raw data of each experiment consisted of 60 fluorescence micrographs acquired at regular intervals including several images acquired before the addition of buffer or agonist. The charts (A-G) each show a quantification of the response seen through all the 60 images, performed as described in analysis method 2. The change in total area of the highly fluorescent aggregates, relative to the initial area of fluorescent aggregates is plotted as the ordinate in all graphs in Figure 3, versus time for each experiment. Scale bar 10 mm.

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Figure 4. Dose response curve (two experiments) for forskolin-induced redistribution of the PKAc-F64L-S65T-GFP fusion.

Figure 5. Time from initiation of a response to half maximal ($t_{1/2max}$) and maximal (t_{max}) PKAc-F64L-S65T-GFP redistribution. The data was extracted from curves such as that shown in "Figure 2." All $t_{1/2max}$ and t_{max} values are given as mean±SD and are based on a total of 26-30 cells from 2-3 independent experiments for each forskolin concentration. Since the observed redistribution is sustained over time, the t_{max} values were taken as the earliest time point at which complete redistribution is reached. Note that the values do not relate to the degree of redistribution.

Figure 6. Parallel dose response analyses of forskolin induced cAMP elevation and PKAc-F64L-S65T-GFP redistribution. The effects of buffer or 5 increasing concentrations of forskolin on the localisation of the PKAc-F64L-S65T-GFP fusion protein in CHO/PKAc-F64L-S65T-GFP cells, grown in a 96 well plate, were analysed as described above. Computing the ratio of the SD's of fluorescence micrographs taken of the same field of cells, prior to and 30 min after the addition of forskolin, gave a reproducible measure of PKAc-F64L-S65T-GFP redistribution. The graph shows the individual 48 measurements and a trace of their mean±s.e.m at each forskolin concentration. For comparison, the effects of buffer or 8 increasing concentrations of forskolin on $[cAMP]_i$ was analysed by a scintillation proximity assay of cells grown under the same conditions. The graph shows a trace of the mean ± s.e.m of 4 experiments expressed in arbitrary units.

Figure 7. BHK cells stably transfected with the human muscarinic (hM1) receptor and the PKCa-F64L-S65T-GFP fusion. Carbachol (100 mM added at 1.0 second) induced a transient redistribution of PKCa-F64L-S65T-GFP from the cytoplasm to the plasma membrane. Images were taken at the following times: a) 1 second before carbachol addition, b) 8.8 seconds after addition and c) 52.8 seconds after addition.

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Figure 8. BHK cells stably transfected with the hM1 receptor and PKCa-F64L-S65T-GFP fusion were treated with carbachol (1 mM, 10 mM, 100 mM). In single cells intracellular [Ca^{2+}] was monitored simultaneously with the redistribution of PKCa-F64L-S65T-GFP. Dashed line indicates the addition times of carbachol. The top panel shows changes in the intracellular Ca^{2+} concentration of individual cells with time for each treatment. The middle panel shows changes in the average cytoplasmic GFP fluorescence for individual cells against time for each treatment. The bottom panel shows changes in the fluorescence of the periphery of single cells, within regions that specifically include the circumferential edge of a cell as seen in normal projection, the regions which offers best chance to monitor changes in the fluorescence intensity of the plasma membrane.

Figure 9. a) The hERK1-F64L-S65T-GFP fusion expressed in HEK293 cells treated with 100 mM of the MEK1 inhibitor PD98059 in HAM F-12 (without serum) for 30 minutes at 37 °C. The nuclei empty of fluorescence during this treatment.

b) The same cells as in (a) following treatment with 10 % foetal calf serum for 15 minutes at 37 °C.

c) Time profiles for the redistribution of GFP fluorescence in HEK293 cells following treatment with various concentrations of EGF in Hepes buffer (HAM F-12 replaced with Hepes buffer directly before the experiment). Redistribution of fluorescence is expressed as the change in the ratio value between areas in nucleus and cytoplasm of single cells. Each time profile is the mean for the changes seen in six single cells.

d) Bar chart for the end-point measurements, 600 seconds after start of EGF treatments, of fluorescence change (nucleus:cytoplasm) following various concentrations of EGF.

Figure 10.

a) The SMAD2-EGFP fusion expressed in HEK293 cells starved of serum overnight in HAM F-12. HAM F-12 was then replaced with Hepes buffer pH 7.2 immediately before the experiment. Scale bar is 10 mm.

b) HEK 293 cells expressing the SMAD2-EGFP fusion were treated with various concentration of TGF-beta as indicated, and the redistribution of fluorescence monitored against time.

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The time profile plots represent increases in fluorescence within the nucleus, normalised to starting values in each cell measured. Each trace is the time profile for a single cell nucleus.

c) A bar chart representing the end-point change in fluorescence within nuclei (after 850 seconds of treatment) for different concentrations of TGF-beta. Each bar is the value for a single nucleus in each treatment.

Figure 11. The VASP-F64L-S65T-GFP fusion in CHO cells stably transfected with the human insulin receptor. The cells were starved for two hours in HAM F-12 without serum, then treated with 10% foetal calf serum. The image shows the resulting redistribution of fluorescence after 15 minutes of treatment. GFP fluorescence becomes localised in structures identified as focal adhesions along the length of actin stress fibres.

Figure 12. Time lapse recording GLUT4-GFP redistribution in CHO-HIR cells. Time indicates minutes after the addition of 100 nM insulin.

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EXAMPLE 1

Construction, testing and implementation of an assay for cAMP based on PKA activation in real time within living cells.

Useful for monitoring the activity of signalling pathways which lead to altered concentrations of cAMP, e.g. activation of G-protein coupled receptors which couple to G-proteins of the G_s or G_i class.

The catalytic subunit of the murine cAMP dependent protein kinase (PKAc)was fused C-terminally to a F64L-S65T derivative of GFP. The resulting fusion (PKAc-F64L-S65T-GFP) was used for monitoring *in vivo* the translocation and thereby the activation of PKA.

Construction of the PKAc-F64L-S65T-GFP fusion:

Convenient restriction endonuclease sites were introduced into the cDNAs encoding murine PKAc (Gen Bank Accession number: M12303) and F64L-S65T-GFP (sequence disclosed in WO 97/11094) by polymerase chain reaction (PCR). The PCR reactions were performed according to standard protocols with the following primers:

5'PKAc: TTggACACAAgCTTTggACACCCTCAggATATgggCAACgCCgCCgCCgCCAAg (SEQ ID NO:3),

3'PKAc: gTCATCTTCTCgAgTCTTTCAggCgCgCCCAAACTCAgTAAACTCCTTgCCACAC (SEQ ID NO:4) ,

5'GFP: TTggACACAAgCTTTggACACggCgCgCCATgAgTAAAggAgAAgAACTTTTC (SEQ ID NO:1),

3'GFP: gTCATCTTCTCgAgTCTTACTCCTgAggTTTgTATAgTTCATCCATgCCATgT (SEQ ID NO:2).

The PKAc amplification product was then digested with HindIII+AscI and the F64L-S65T-GFP product with AscI+XhoI. The two digested PCR products were subsequently ligated with a HindIII+XhoI digested plasmid (pZeoSV® mammalian expression vector, Invitrogen, San Diego, CA, USA). The resulting fusion construct (SEQ ID NO:68 & 69) was under control of the SV40 promoter.

Transfection and cell culture conditions.

Chinese hamster ovary cells (CHO), were transfected with the plasmid containing the PKAc-F64L-S65T-GFP fusion using the calcium phosphate precipitate method in HEPES-buffered saline (Sambrook *et al.*, 1989). Stable transfectants were selected using 1000 mg Zeocin/ml (Invitrogen) in the growth medium (DMEM with 1000 mg glucose/l, 10 % fetal bovine serum (FBS), 100 mg penicillin-streptomycin mixture ml^{-1}, 2 mM L-glutamine purchased from Life Technologies Inc., Gaithersburg, MD, USA). Untransfected CHO cells were used as the control. To assess the effect of glucagon on fusion protein translocation, the PKAc-F64L-S65T-GFP fusion was stably expressed in baby hamster kidney cells overexpressing the human glucagon receptor (BHK/GR cells) Untransfected BHK/GR cells were used as the control. Expression of GR was maintained with 500 mg G418/ml (*Neo* marker) andPKAc-F64L-S65T-GFP was maintained with 500 mg Zeocin/ml (*Sh ble* marker). CHO cells were also simultaneously co-transfected with vectors containing the PKAc-F64L-S65T-GFP fusion and the human a2a adrenoceptor (hARa2a).

For fluorescence microscopy, cells were allowed to adhere to Lab-Tek chambered coverglasses (Nalge Nunc Int., Naperville, IL, USA) for at least 24 hours and cultured to about 80% confluence. Prior to experiments, the cells were cultured over night without selection pressure in HAM F-12 medium with glutamax (Life Technologies), 100 mg penicillin-streptomycin mixture ml^{-1} and 0.3 % FBS. This medium has low autofluorescence enabling fluorescence microscopy of cells straight from the incubator.

Monitoring activity of PKA activity in real time:

Image aquisition of live cells were gathered using a Zeiss Axiovert 135M fluorescence microscope fitted with a Fluar 40X, NA: 1.3 oil immersion objective and coupled to a Photometrics CH250 charged coupled device (CCD) camera. The cells were illuminated with a 100 W HBO arc lamp. In the light path was a 470±20 nm excitation filter, a 510 nm dichroic mirror

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and a 515±15 nm emission filter for minimal image background. The cells were kept and monitored to be at 37°C with a custom built stage heater.

Images were processed and analyzed in the following manner:.

Method 1: Stepwise procedure for quantitation of translocation of PKA:

1. The image was corrected for dark current by performing a pixel-by-pixel subtraction of a dark image (an image taken under the same conditions as the actual image, except the camera shutter is not allowed to open).

2. The image was corrected for non-uniformity of the illumination by performing a pixel-by-pixel ratio with a flat field correction image (an image taken under the same conditions as the actual image of a uniformly fluorescent specimen).

3. The image histogram, i.e., the frequency of occurrence of each intensity value in the image, was calculated.

4. A smoothed, second derivative of the histogram was calculated and the second zero is determined. This zero corresponds to the inflection point of the histogram on the high side of the main peak representing the bulk of the image pixel values.

5. The value determined in step 4 was subtracted from the image. All negative values were discarded.

6. The variance (square of the standard deviation) of the remaining pixel values was determined. This value represents the "response" for that image.

7. Scintillation proximity assay (SPA) for independent quantitation of cAMP:

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Method 2: Alternative method for quantitation of PKA redistribution:

1. The fluorescent aggregates are segmented from each image using an automatically found threshold based on the maximisation of the information measure between the object and background. The *a priori* entropy of the image histogram is used as the information measure.

2. The area of each image occupied by the aggregates is calculated by counting pixels in the segmented areas.

3. The value obtained in step 2 for each image in a series, or treatment pair, is normalised to the value found for the first (unstimulated) image collected. A value of zero (0) indicates no redistribution of fluorescence from the starting condition. A value of one (1) by this method equals full redistribution.

Cells were cultured in HAM F-12 medium as described above, but in 96-well plates. The medium was exchanged with Ca^{2+}-HEPES buffer including 100 mM IBMX and the cells were stimulated with different concentrations of forskolin for 10 min. Reactions were stopped with addition of NaOH to 0.14 M and the amount of cAMP produced was measured with the cAMP-SPA kit, RPA538 (Amersham) as described by the manufacturer.

Manipulating intracellular levels of cAMP to test the PKAc-F64L-S65T-GFP fusion.

The following compounds were used to vary cAMP levels: Forskolin, an activator of adenylate cyclase; dbcAMP, a membrane permeable cAMP analog which is not degraded by phosphodiesterase; IBMX, an inhibitor of phosphodiesterase.

CHO cells stably expressing the PKAc-F64L-S65T-GFP, showed a dramatic translocation of the fusion protein from a punctate distribution to an even distribution throughout the cytoplasm following stimulation with 1 mM forskolin (n=3), 10 mM forskolin (n=4) and 50 mM forskolin (n=4) (Fig 1), or dbcAMP at 1mM (n=6).

Fig. 2 shows the progression of response in time following treatment with 1 mM forskolin.

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Fig. 3 gives a comparison of the average temporal profiles of fusion protein redistribution and a measure of the extent of each response to the three forskolin concentrations (Fig. 3A, E, B), and to 1 mM dbcAMP (fig 3C) which caused a similar but slower response, and to addition of 100 mM IBMX (n=4, Fig. 3D) which also caused a slow response, even in the absence of adenylate cyclase stimulation. Addition of buffer (n=2) had no effect (data not shown).

As a control for the behavior of the fusion protein, F64L-S65T-GFP alone was expressed in CHO cells and these were also given 50 mM forskolin (n=5); the uniform diffuse distribution characteristic of GFP in these cells was unaffected by such treatment (data not shown).

The forskolin induced translocation of PKAc-F64L-S65T-GFP showed a dose-response relationship (Fig 4 and 6), see quantitative procedures above.

Reversibility of PKAc-F64L-S65T-GFP translocation.

The release of the PKAc probe from its cytoplasmic anchoring hotspots was reversible. Washing the cells repeatedly (5-8 times) with buffer after 10μM forskolin treatment completely restored the punctate pattern within 2-5 min (n=2, Fig. 3E). In fact the fusion protein returned to a pattern of fluorescent cytoplasmic aggregates virtually indistinguishable from that observed before forskolin stimulation.

To test whether the return of fusion protein to the cytoplasmic aggregates reflected a decreased $[cAMP]_i$, cells were treated with a combination of 10 mM forskolin and 100 mM IBMX (n=2) then washed repeatedly (5-8 times) with buffer containing 100 mM IBMX (Fig. 3F). In these experiments, the fusion protein did not return to its prestimulatory localization after removal of forskolin.

Testing the PKA-F64L-S65T-GFP probe with physiologically relevant agents.

To test the probe's response to receptor activation of adenylate cyclase, BHK cells stably transfected with the glucagon receptor and the PKA-F64L-S65T-GFP probe were exposed to glucagon stimulation. The glucagon receptor is coupled to a G_s protein which activates adenylate cyclase, thereby increasing the cAMP level. In these cells, addition of 100 nM glucagon (n=2) caused the release of the PKA-F64L-S65T-GFP probe from the cytoplasmic aggregates and a resulting translocation of the fusion protein to a more even cytoplasmic

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distribution within 2-3 min (Fig. 3G). Similar but less pronounced effects were seen at lower glucagon concentrations (n=2, data not shown). Addition of buffer (n=2) had no effect over time (data not shown).

Transiently transfected CHO cells expressing hARa2a and the PKA-F64L-S65T-GFP probe were treated with 10 mM forskolin for 7.5 minutes, then, in the continued presence of forskolin, exposed to 10 mM norepinephrine to stimulate the exogenous adrenoreceptors, which couple to a G_i protein, which inhibit adenylate cyclase. This treatment led to reappearance of fluorescence in the cytoplasmic aggregates indicative of a decrease in $[cAMP]_i$ (Fig. 3H).

Fusion protein translocation correlated with $[cAMP]_i$

As described above, the time it took for a response to come to completion was dependent on the forskolin dose (Fig. 5) In addition the degree of responses was also dose dependent. To test the PKA-F64L-S65T-GFP fusion protein translocation in a semi high through-put system, CHO cells stably transfected with the PKA-F64L-S65T-GFP fusion was stimulated with buffer and 5 increasing doses of forskolin (n=8). Using the image analysis algorithm described above (Method 1), a dose response relationship was observed in the range from 0.01-50 mM forskolin (Fig. 6). A half maximal stimulation was observed at about 2 mM forskolin. In parallel, cells were stimulated with buffer and 8 increasing concentrations of forskolin (n=4) in the range 0.01-50 mM. The amount of cAMP produced was measured in an SPA assay. A steep increase was observed between 1 and 5 mM forskolin coincident with the steepest part of the curve for fusion protein translocation (also Fig. 6)

EXAMPLE 2

Quantitation of redistribution in real-time within living cells.

Probe for detection of PKC activity in real time within living cells:

Construction of PKC-GFP fusion:

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The probe was constructed by ligating two restriction enzyme treated polymerase chain reaction (PCR) amplification products of the cDNA for murine PKCα (GenBank Accession number: M25811) and F64L-S65T-GFP (sequence disclosed in WO 97/11094) respectively. Taq® polymerase and the following oligonucleotide primers were used for PCR;

5'mPKCa: TTggACACAAgCTTTggACACCCTCAggATATggCTgACgTTTACCCggCCAACg (SEQ ID NO:5),

3'mPKCa: gTCATCTTCTCgAgTCTTTCAggCgCgCCCTACTgCACTTTgCAAgATTgggTgC (SEQ ID NO:6),

5'F64L-S65T-GFP: TTggACACAAgCTTTggACACggCgCgCCATgAgTAAAggAgAAgAACTTTTC (SEQ ID NO:1),

3'F64L-S65T-GFP: gTCATCTTCTCgAgTCTTACTCCTgAggTTTgTATAgTTCATCCATgCCATgT (SEQ ID NO:2).

The hybrid DNA strand was inserted into the pZeoSV® mammalian expression vector as a HindIII-XhoI casette as described in example 1.

Cell Culture:

BHK cells expressing the human M1 receptor under the control of the inducible metallothionine promoter and maintained with the dihydrofolate reductase marker were transfected with the PKCα-F64L-S65T-GFP probe using the calcium phosphate precipitate method in HEPES buffered saline (HBS [pH 7.10]). Stable transfectants were selected using 1000 µg Zeocin®/ml in the growth medium (DMEM with 1000 mg glucose/l, 10 % foetal bovine serum (FBS), 100 mg penicillin-streptomycin mixture ml-1, 2 mM l-glutamine). The hM1 receptor and PKCα-F64L-S65T-GFP fusion protein were maintained with 500 nM methotrexate and 500 µg Zeocin®/ml respectively. 24 hours prior to any experiment, the cells were transferred to HAM F-12 medium with glutamax, 100 µg penicillin-streptomycin mixture ml^{-1} and 0.3 % FBS. This medium relieves selection pressure, gives a low induction of signal transduction pathways and has a low autofluorescence at the relevant wavelength enabling fluorescence microscopy of cells straight from the incubator.

Monitoring the PKC activity in real time:

Digital images of live cells were gathered using a Zeiss Axiovert 135M fluorescence microscope fitted with a 40X, NA: 1.3 oil immersion objective and coupled to a Photometrics

CH250 charged coupled device (CCD) camera. The cells were illuminated with a 100 W arc lamp. In the light path was a 470±20 nm excitation filter, a 510 nm dichroic mirror and a 515±15 nm emission filter for minimal image background. The cells were kept and monitored to be at 37°C with a custom built stage heater.

Images were analyzed using the IPLab software package for Macintosh.

Upon stimulation of the M1-BHK cells, stably expressing the PKCα-F64L-S65T-GFP fusion, with carbachol we observed a dose-dependent transient translocation from the cytoplasm to the plasma membrane (Fig. 7a,b,c). Simultaneous measurement of the cytosolic free calcium concentration shows that the carbachol-induced calcium mobilisation precedes the translocation (Fig. 8).

Stepwise procedure for quantitation of translocation of PKC:

1. The image was corrected for dark current by performing a pixel-by-pixel subtraction of a dark image (an image taken under the same conditions as the actual image, except the camera shutter is not allowed to open).

2. The image was corrected for non-uniformity of the illumination by performing a pixel-by-pixel ratio with a flat field correction image (an image taken under the same conditions as the actual image of a uniformly fluorescent specimen).

3. A copy of the image was made in which the edges are identified. The edges in the image are found by a standard edge-detection procedure – convolving the image with a kernel which removes any large-scale unchanging components (i.e., background) and accentuates any small-scale changes (i.e., sharp edges). This image was then converted to a binary image by threshholding. Objects in the binary image which are too small to represent the edges of cells were discarded. A dilation of the binary image was performed to close any gaps in the image edges. Any edge objects in the image which were in contact with the borders of the image are discarded. This binary image represents the edge mask.

4. Another copy of image was made via the procedure in step 3. This copy was further processed to detect objects which enclose "holes" and setting all pixels inside the holes to the binary value of the edge, i.e., one. This image represents the whole cell mask.

5. The original image was masked with the edge mask from step 3 and the sum total of all pixel values is determined.

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6. The original image was masked with the whole cell mask from step 4 and the sum total of all pixel values was determined.

7. The value from step 5 was divided by the value from step 6 to give the final result, the fraction of fluorescence intensity in the cells which was localized in the edges.

EXAMPLE 3

Probes for detection of mitogen activated protein kinase Erk1 redistribution.

Useful for monitoring signalling pathways involving MAPK, e.g. to identify compounds which modulate the activity of the pathway in living cells.

Erk1, a serine/threonine protein kinase, is a component of a signalling pathway which is activated by e.g. many growth factors.

Probes for detection of ERK-1 activity in real time within living cells:

The extracellular signal regulated kinase (ERK-1, a mitogen activated protein kinase, MAPK) is fused N- or C-terminally to a derivative of GFP. The resulting fusions expressed in different mammalian cells are used for monitoring *in vivo* the nuclear translocation, and thereby the activation, of ERK1 in response to stimuli that activate the MAPK pathway.

a) Construction of murine ERK1 - F64L-S65T-GFP fusion:

Convenient restriction endonuclease sites are introduced into the cDNAs encoding murine ERK1 (GenBank Accession number: Z14249) and F64L-S65T-GFP (sequence disclosed in WO 97/11094) by polymerase chain reaction (PCR). The PCR reactions are performed according to standard protocols with the following primers:

5'ERK1: TTggACACAAgCTTTggACACCCTCAggATATggCggCggCggCggCggCTCCggggggCgggg (SEQ ID NO:7),

3'ERK1: gTCATCTTCTCgAgTCTTTCAggCgCgCCCggggCCCTCTggCgCCCCTggCTgg (SEQ ID NO:8),

5'F64L-S65T-GFP: TTggACACAAgCTTTggACACggCgCgCCATgAgTAAAggAgAAgAACTTTTC (SEQ ID NO:1)

3'F64L-S65T-GFP: gTCATCTTCTCgAgTCTTACTCCTgAggTTTgTATAgTTCATCCATgCCATgT (SEQ ID NO:2)

To generate the mERK1-F64L-S65T-GFP (SEQ ID NO:56 & 57) fusion the ERK1 amplification product is digested with HindIII+AscI and the F64L-S65T-GFP product with AscI+XhoI. To generate the F64L-S65T-GFP-mERK1 fusion the ERK1 amplification product is then digested with HindIII+Bsu36I and the F64L-S65T-GFP product with Bsu36I+XhoI.The two pairs of digested PCR products are subsequently ligated with a HindIII+XhoI digested plasmid (pZeoSV® mammalian expression vector, Invitrogen, San Diego, CA, USA). The resulting fusion constructs are under control of the SV40 promoter.

b) The human Erk1 gene (GenBank Accession number: X60188) was amplified using PCR according to standard protocols with primers Erk1-top (SEQ ID NO:9) and Erk1-bottom/+stop (SEQ ID NO:10) . The PCR product was digested with restriction enzymes EcoR1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with EcoR1 and BamH1. This produces an EGFP-Erk1 fusion (SEQ ID NO:38 &39) under the control of a CMV promoter.

The plasmid containing the EGFP-Erk1 fusion was transfected into HEK293 cells employing the FUGENE transfection reagent (Boehringer Mannheim). Prior to experiments the cells were grown to 80%-90% confluency 8 well chambers in DMEM with 10% FCS. The cells were washed in plain HAM F-12 medium (without FCS), and then incubated for 30-60 minutes in plain HAM F-12 (without FCS) with 100 micromolar PD98059, an inhibitor of MEK1, a kinase which activates Erk1; this step effectively empties the nucleus of EGFP-Erk1. Just before starting the experiment, the HAM F-12 was replaced with Hepes buffer following a wash with Hepes buffer. This removes the PD98059 inhibitor; if blocking of MEK1 is still wanted (e.g. in control experiments), the inhibitor is included in the Hepes buffer.

The experimental setup of the microscope was as described in example 1.

60 images were collected with 10 seconds between each, and with the test compound added after image number 10.

Addition of EGF (1-100 nM) caused within minutes a redistribution of EGFP-Erk1 from the cytoplasm into the nucleus (Fig. 9a,b).

The response was quantitated as described below and a dose-dependent relationship between EGF concentration and nuclear translocation of EGFP-Erk1 was found (Fig. 9c,d). Reditribution of GFP fluorescence is expressed in this example as the change in the ratio value between areas in nuclear versus cytoplasmic compartments of the cell. Each time profile is the average of nuclear to cytoplasmic ratios from six cells in each treatment.

EXAMPLE 4:

Probes for detection of Erk2 redistribution.

Useful for monitoring signalling pathways involving MAPK, e.g. to identify compounds which modulate the activity of the pathway in living cells.

Erk2, a serine/threonine protein kinase, is closely related to Erk1 but not identical; it is a component of a signalling pathway which is activated by e.g. many growth factors.

a) The rat Erk2 gene (GenBank Accession number: M64300) was amplified using PCR according to standard protocols with primers Erk2-top (SEQ ID NO:11) and Erk2-bottom/+stop (SEQ ID NO:13) The PCR product was digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Xho1 and BamH1. This produces an EGFP-Erk2 fusion (SEQ ID NO:40 &41) under the control of a CMV promoter.

b) The rat Erk2 gene (GenBank Accession number: M64300) was amplified using PCR according to standard protocols with primers (SEQ ID NO:11) Erk2-top and Erk2-bottom/-stop (SEQ ID NO:12). The PCR product was digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with Xho1 and BamH1. This produces an Erk2-EGFP fusion (SEQ ID NO:58 &59) under the control of a CMV promoter.

The resulting plasmids were transfected into CHO cells and BHK cells. The cells were grown under standard conditions. Prior to experiments, the cells were starved in medium without serum for 48-72 hours. This led to a predominantly cytoplasmic localization of both probes, especially in BHK cells. 10% fetal calf serum was added to the cells and the fluorescence of the cells was recorded as explained in example 3. Addition of serum caused the probes to redistribute into the nucleus within minutes of addition of serum.

EXAMPLE 5:

Probes for detection of Smad2 redistribution.

Useful for monitoring signalling pathways activated by some members of the transforming growth factor-beta family, e.g. to identify compounds which modulate the activity of the pathway in living cells.

Smad 2, a signal transducer, is a component of a signalling pathway which is induced by some members of the TGFbeta family of cytokines.

a) The human Smad2 gene (GenBank Accession number: AF027964) was amplified using PCR according to standard protocols with primers Smad2-top (SEQ ID NO:24) and Smad2-bottom/+stop (SEQ ID NO:26) . The PCR product was digested with restriction enzymes EcoR1 and Acc65I, and ligated into pEGFP-C1 (Clontech; Palo Alto; GenBank Accession number U55763) digested with EcoR1 and Acc65I. This produces an EGFP-Smad2 fusion (SEQ ID NO:50&51) under the control of a CMV promoter.

b) The human Smad2 gene (GenBank Accession number: AF027964) was amplified using PCR according to standard protocols with primers Smad2-top (SEQ ID NO:24) and Smad2-bottom/-stop (SEQ ID NO:25) . The PCR product was digested with restriction enzymes EcoR1 and Acc65I, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with EcoR1 and Acc65I. This produces a Smad2-EGFP fusion (SEQ ID NO:74 &75) under the control of a CMV promoter.

The plasmid containing the EGFP-Smad2 fusion was transfected into HEK293 cells, where it showed a cytoplasmic distribution. Prior to experiments the cells were grown in 8 well Nunc

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chambers in DMEM with 10% FCS to 80% confluency and starved overnight in HAM F-12 medium without FCS.

For experiments, the HAM F-12 medium was replaced with Hepes buffer pH 7.2.

The experimental setup of the microscope was as described in example 1.

90 images were collected with 10 seconds between each, and with the test compound added after image number 5.

After serum starvation of cells, each nucleus contains less GFP fluorescence than the surrounding cytoplasm (Fig. 10a). Addition of TGFbeta caused within minutes a redistribution of EGFP-Smad2 from the cytoplasma into the nucleus (Fig. 10b).

The redistribution of fluorescence within the treated cells was quantified simply as the fractional increase in nuclear fluorescence normalised to the starting value of GFP fluorescence in the nucleus of each unstimulated cell.

EXAMPLE 6:

Probe for detection of VASP redistribution.

Useful for monitoring signalling pathways involving rearrangement of cytoskeletal elements, e.g. to identify compounds which modulate the activity of the pathway in living cells.

VASP, a phosphoprotein, is a component of cytoskeletal structures, which redistributes in response to signals which affect focal adhesions.

a) The human VASP gene (GenBank Accession number: Z46389) was amplified using PCR according to standard protocols with primers VASP-top (SEQ ID NO:94) and VASP-bottom/+stop (SEQ ID NO:95). The PCR product was digested with restriction enzymes Hind3 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Hind3and BamH1. This produces an EGFP-VASP fusion (SEQ ID NO:124 &125) under the control of a CMV promoter.

The resulting plasmid was transfected into CHO cells expressing the human insulin receptor using the calcium-phosphate transfection method. Prior to experiments, cells were grown in 8 well Nunc chambers and starved overnight in medium without FCS.

Experiments are performed in a microscope setup as described in example 1.

10% FCS was added to the cells and images were collected. The EGFP-VASP fusion was redistributed from a somewhat even distribution near the periphery into more localized structures, identified as focal adhesion points (Fig. 11).

A large number of further GFP fusions have been made or are in the process of being made, as apparent from the following Examples 7-22 which also suggest suitable host cells and substances for activation of the cellular signalling pathways to be monitored and analyzed.

EXAMPLE 7:

Probe for detection of actin redistribution.

Useful for monitoring signalling pathways involving rearrangement or formation of actin filaments, e.g. to identify compounds which modulate the activity of pathways leading to cytoskeletal rearrangements in living cells.

Actin is a component of cytoskeletal structures, which redistributes in response to very many cellular signals.

The actin binding domain of the human alpha-actinin gene (GenBank Accession number: X15804) was amplified using PCR according to standard protocols with primers ABD-top (SEQ ID NO:90) and ABD-bottom/-stop (SEQ ID NO:91). The PCR product was digested with restriction enzymes Hind3 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with Hind3 and BamH1. This produced an actin-binding-domain-EGFP fusion (SEQ ID NO:128 &129) under the control of a CMV promoter.

The resulting plasmid was transfected into CHO cells expressing the human insulin receptor. Cells were stimulated with insulin which caused the actin binding domain-EGFP probe to become redistributed into morphologically distinct membrane-associated structures.

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Example 8:

Probes for detection of p38 redistribution.

Useful for monitoring signalling pathways responding to various cellular stress situations, e.g. to identify compounds which modulate the activity of the pathway in living cells, or as a counterscreen.

p38, a serine/thronine protein kinase, is a component of a stress-induced signalling pathway which is activated by many types of cellular stress, e.g. TNFalpha, anisomycin, UV and mitomycin C.

a) The human p38 gene (GenBank Accession number: L35253) was amplified using PCR according to standard protocols with primers p38-top (SEQ ID NO:14) and p38-bottom/+stop (SEQ ID NO: 16). The PCR product was digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Xho1 and BamH1. This produced an EGFP-p38 fusion (SEQ ID NO:46 &47) under the control of a CMV promoter.

b) The human p38 gene (GenBank Accession number: L35253) was amplified using PCR according to standard protocols with primers p38-top (SEQ ID NO:13) and p38-bottom/-stop (SEQ ID NO:15) . The PCR product was digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with Xho1 and BamH1. This produced a p38-EGFP fusion (SEQ ID NO:64 &65) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. HEK293, in which the EGFP-p38 probe and/or the p38-EGFP probe should change its cellular distribution from predominantly cytoplasmic to nuclear within minutes in response to activation of the signalling pathway with e.g. anisomycin.

Example 9:

Probes for detection of Jnk1 redistribution.

Useful for monitoring signalling pathways responding to various cellular stress situations, e.g. to identify compounds which modulate the activity of the pathway in living cells, or as a counterscreen.

Jnk1, a serine/threonine protein kinase, is a component of a stress-induced signalling pathway different from the p38 described above, though it also is activated by many types of cellular stress, e.g. TNFalpha, anisomycin and UV.

a) The human Jnk1 gene (GenBank Accession number: L26318) was amplified using PCR according to standard protocols with primers Jnk-top (SEQ ID NO:17) and Jnk-bottom/+stop (SEQ ID NO:19) . The PCR product was digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Xho1 and BamH1. This produced an EGFP-Jnk1 fusion (SEQ ID NO:44 &45) under the control of a CMV promoter.

b) The human Jnk1 gene (GenBank Accession number: L26318) was amplified using PCR according to standard protocols with primers Jnk-top (SEQ ID NO:17) and Jnk-bottom/-stop (SEQ ID NO:18) . The PCR product was digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with Xho1 and BamH1. This produced a Jnk1-EGFP fusion (SEQ ID NO:62 &63) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. HEK293, in which the EGFP-Jnk1 probe and/or the Jnk1-EGFP probe should change its cellular distribution from predominantly cytoplasmic to nuclear in response to activation of the signalling pathway with e.g. anisomycin.

Example 10:

Probes for detection of PKG redistribution.

Useful for monitoring signalling pathways involving changes in cyclic GMP levels, e.g. to identify compounds which modulate the activity of the pathway in living cells.

PGK, a cGMP-dependent serine/threonine protein kinase, mediates the guanylyl-cyclase/cGMP signal.

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a) The human PKG gene (GenBank Accession number: Y07512) is amplified using PCR according to standard protocols with primers PKG-top (SEQ ID NO:81) and PKG-bottom/+stop (SEQ ID NO:83) . The PCR product is digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Xho1 and BamH1. This produces an EGFP-PKG fusion (SEQ ID NO:134 &135) under the control of a CMV promoter.

b) The human PKG gene (GenBank Accession number: Y07512) is amplified using PCR according to standard protocols with primers PKG-top (SEQ ID NO:81) and PKG-bottom/-stop (SEQ ID NO: 82) . The PCR product is digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with Xho1 and BamH1. This produces a PKG-EGFP fusion (SEQ ID NO:136 &137) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. A10, in which the EGFP-PKG probe and/or the PKG-EGFP probe should change its cellular distribution from cytoplasmic to one associated with cytoskeletal elements within minutes in response to treatment with agents which raise nitric oxide (NO) levels.

Example 11:

Probes for detection of IkappaB kinase redistribution.

Useful for monitoring signalling pathways leading to NFkappaB activation, e.g. to identify compounds which modulate the activity of the pathway in living cells.

IkappaB kinase, a serine/threonine kinase, is a component of a signalling pathway which is activated by a variety of inducers including cytokines, lymphokines, growth factors and stress.

a) The alpha subunit of the human IkappaB kinase gene (GenBank Accession number: AF009225) is amplified using PCR according to standard protocols with primers IKK-top (SEQ ID NO:96) and IKK-bottom/+stop (SEQ ID NO:98). The PCR product is digested with restriction enzymes EcoR1 and Acc65I, and ligated into pEGFP-C1 (Clontech, Palo Alto;

GenBank Accession number U55763) digested with EcoR1and Acc65I. This produces an EGFP-IkappaB-kinase fusion (SEQ ID NO:120 &121) under the control of a CMV promoter.

b) The alpha subunit of the human IkappaB kinase gene (GenBank Accession number: AF009225) is amplified using PCR according to standard protocols with primers IKK-top (SEQ ID NO:96) and IKK-bottom/-stop (SEQ ID NO:97). The PCR product is digested with restriction enzymes EcoR1 and Acc65I, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with EcoR1 and Acc65I. This produces an IkappaB-kinase-EGFP fusion (SEQ ID NO:122 &123) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. Jurkat, in which the EGFP-IkappaB-kinase probe and/or the IkappaB-kinase-EGFP probe should achieve a more cytoplasmic distribution within seconds following stimulation with e.g. TNFalpha.

Example 12:

Probes for detection of CDK2 redistribution.

Useful for monitoring signalling pathways of the cell cycle, e.g. to identify compounds which modulate the activity of the pathway in living cells.

CDK2, a cyclin-dependent serine/threonine kinase, is a component of the signalling system which regulates the cell cycle.

a) The human CDK2 gene (GenBank Accession number: X61622) is amplified using PCR according to standard protocols with primers CDK2-top (SEQ ID NO:102) and CDK2-bottom/+stop (SEQ ID NO: 104). The PCR product is digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Xho1 and BamH1. This produces an EGFP-CDK2 fusion (SEQ ID NO:114 &115) under the control of a CMV promoter.

b) The human CDK2 gene (GenBank Accession number: X61622) is amplified using PCR according to standard protocols with primers CDK2-top (SEQ ID NO:102) and CDK2-bottom/-stop (SEQ ID NO:103). The PCR product is digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with Xho1 and BamH1. This produces a CDK2-EGFP fusion (SEQ ID NO:112 &113) under the control of a CMV promoter.

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The resulting plasmids are transfected into a suitable cell line, e.g. HEK293 in which the EGFP-CDK2 probe and/or the CDK2-EGFP probe should change its cellular distribution from cytoplasmic in contact-inhibited cells, to nuclear location in response to activation with a number of growth factors, e.g. IGF.

Example 13:

Probes for detection of Grk5 redistribution.

Useful for monitoring signalling pathways involving desensitization of G-protein coupled receptors, e.g. to identify compounds which modulate the activity of the pathway in living cells.

Grk5, a G-protein coupled receptor kinase, is a component of signalling pathways involving membrane bound G-protein coupled receptors.

a) The human Grk5 gene (GenBank Accession number: L15388) is amplified using PCR according to standard protocols with primers Grk5-top (SEQ ID NO:27) and Grk5-bottom/+stop (SEQ ID NO:29). The PCR product is digested with restriction enzymes EcoR1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with EcoR1 and BamH1. This produces an EGFP-Grk5 fusion (SEQ ID NO:42 &43) under the control of a CMV promoter.

b) The human Grk5 gene (GenBank Accession number: L15388) is amplified using PCR according to standard protocols with primers Grk5-top (SEQ ID NO:27) and Grk5-bottom/-stop (SEQ ID NO:28). The PCR product is digested with restriction enzymes EcoR1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with EcoR1 and BamH1. This produces a Grk5-EGFP fusion (SEQ ID NO:60 &61) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. HEK293 expressing a rat dopamine D1A receptor, in which the EGFP-Grk5 probe and/or the Grk5-EGFP probe should change its cellular distribution from predominantly cytoplasmic to peripheral in response to activation of the signalling pathway with e.g. dopamine.

Example 14:

Probes for detection of Zap70 redistribution.

Useful for monitoring signalling pathways involving the T cell receptor, e.g. to identify compounds which modulate the activity of the pathway in living cells.

Zap70, a tyrosine kinase, is a component of a signalling pathway which is active in e.g. T-cell differentiation.

a) The human Zap70 gene (GenBank Accession number: L05148) is amplified using PCR according to standard protocols with primers Zap70-top (SEQ ID NO:105) and Zap70-bottom/+stop (SEQ ID NO:107). The PCR product is digested with restriction enzymes EcoR1 and BamH1, and ligated into pEGFP-C1 (GenBank Accession number U55763) digested with EcoR1 and BamH1. This produces an EGFP-Zap70 fusion (SEQ ID NO:108 &109) under the control of a CMV promoter.

b) The human Zap70 gene (GenBank Accession number: L05148) is amplified using PCR according to standard protocols with primers Zap70-top (SEQ ID NO:105) and Zap70-bottom/-stop (SEQ ID NO:106). The PCR product is digested with restriction enzymes EcoR1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with EcoR1 and BamH1. This produces a Zap70-EGFP fusion (SEQ ID NO:110 &111) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. Jurkat, in which the EGFP-Zap70 probe and/or the Zap70-EGFP probe should change its cellular distribution from cytoplasmic to membrane-associated within seconds in response to activation of the T cell receptor signalling pathway with e.g. antibodies to CD3epsilon.

Example 15:

Probes for detection of p85 redistribution.

Useful for monitoring signalling pathways involving PI-3 kinase, e.g. to identify compounds which modulate the activity of the pathway in living cells.

p85alpha is the regulatory subunit of PI3-kinase which is a component of many pathways involving membrane-bound tyrosine kinase receptors and G-protein-coupled receptors.

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a) The human p85alpha gene (GenBank Accession number: M61906) was amplified using PCR according to standard protocols with primers p85-top-C (SEQ ID NO:22) and p85-bottom/+stop (SEQ ID NO:23) . The PCR product was digested with restriction enzymes Bgl2 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Bgl2 and BamH1. This produced an EGFP-p85alpha fusion (SEQ ID NO:48 &49) under the control of a CMV promoter.

b) The human p85alpha gene (GenBank Accession number: M61906) was amplified using PCR according to standard protocols with primers p85-top-N (SEQ ID NO:20) and p85-bottom/-stop (SEQ ID NO:21) . The PCR product was digested with restriction enzymes E-coR1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with EcoR1 and BamH1. This produced a p85alpha-EGFP fusion (SEQ ID NO:66 &67) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. CHO expressing the human insulin receptor, in which the EGFP-p85 probe and/or the p85-EGFP probe may change its cellular distribution from cytoplasmic to membrane-associated within minutes in response to activation of the receptor with insulin.

Example 16:

Probes for detection of protein-tyrosine phosphatase redistribution.

Useful for monitoring signalling pathways involving tyrosine kinases, e.g. to identify compounds which modulate the activity of the pathway in living cells.

Protein-tyrosine phosphatase1C, a tyrosine-specific phosphatase, is an inhibitory component in signalling pathways involving e.g. some growth factors.

a) The human protein-tyrosine phosphatase 1C gene (GenBank Accession number: X62055) is amplified using PCR according to standard protocols with primers PTP-top (SEQ ID NO:99) and PTP-bottom/+stop (SEQ ID NO:101). The PCR product is digested with restriction enzymes Xho1 and EcoR1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Xho1 and EcoR1. This produces an EGFP-PTP fusion (SEQ ID NO:116 &117) under the control of a CMV promoter.

b) The human protein-tyrosine phosphatase 1C gene (GenBank Accession number: X62055) is amplified using PCR according to standard protocols with primers PTP-top (SEQ ID NO:99) and PTP-bottom/-stop (SEQ ID NO:100). The PCR product is digested with restriction enzymes Xho1 and EcoR1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with Xho1 and EcoR1. This produces a PTP-EGFP fusion (SEQ ID NO:118 &119) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. MCF-7 in which the EGFP-PTP probe and/or the PTP-EGFP probe should change its cellular distribution from cytoplasm to the plasma menbrane within minutes in response to activation of the growth inhibitory signalling pathway with e.g. somatostatin.

Example 17:

Probes for detection of Smad4 redistribution.

Useful for monitoring signalling pathways involving most members of the transforming growth factor-beta family, e.g. to identify compounds which modulate the activity of the pathway in living cells.

Smad4, a signal transducer, is a common component of signalling pathways induced by various members of the TGFbeta family of cytokines.

a) The human Smad4 gene (GenBank Accession number: U44378) was amplified using PCR according to standard protocols with primers Smad4-top and Smad4-bottom/+stop (SEQ ID NO:35) . The PCR product was digested with restriction enzymes EcoR1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with EcoR1 and BamH1. This produce an EGFP-Smad4 fusion (SEQ ID NO:52 &53) under the control of a CMV promoter.

b) The human Smad4 gene (GenBank Accession number: U44378) was amplified using PCR according to standard protocols with primers Smad4-top (SEQ ID NO:33) and Smad4-bottom/-stop (SEQ ID NO:34). The PCR product was digested with restriction enzymes EcoR1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with EcoR1 and BamH1. This produced a Smad4-EGFP fusion (SEQ ID NO:76 &77) under the control of a CMV promoter.

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The resulting plasmids are transfected into a cell line, e.g. HEK293 in which the EGFP-Smad4 probe and/or the Smad4-EGFP probe should change its cellular distribution within minutes from cytoplasmic to nuclear in response to activation of the signalling pathway with e.g. TGFbeta.

Example 18:

Probes for detection of Stat5 redistribution.

Useful for monitoring signalling pathways involving the activation of tyrosine kinases of the Jak family, e.g. to identify compounds which modulate the activity of the pathway in living cells.

Stat5, signal transducer and activator of transcription, is a component of signalling pathways which are induced by e.g. many cytokines and growth factors.

a) The human Stat5 gene (GenBank Accession number: L41142) was amplified using PCR according to standard protocols with primers Stat5-top (SEQ ID NO:30) and Stat5-bottom/+stop (SEQ ID NO:32). The PCR product was digested with restriction enzymes Bgl2 and Acc65I, and ligated into pEGFP-C1 (Clontech; Palo Alto; GenBank Accession number U55763) digested with Bgl2 and Acc65I. This produced an EGFP-Stat5 fusion (SEQ ID NO:54 &55) under the control of a CMV promoter.

b) The human Stat5 gene (GenBank Accession number: L41142) was amplified using PCR according to standard protocols with primers Stat5-top (SEQ ID NO:30) and Stat5-bottom/-stop (SEQ ID NO:331). The PCR product was digested with restriction enzymes Bgl2 and Acc65I, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with Bgl2 and Acc65I. This produced a Stat5-EGFP fusion (SEQ ID NO:78 &79) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. MIN6 in which the EGFP-Stat5 probe and/or the Stat5-EGFP probe should change its cellular distribution from cytoplasmic to nuclear within minutes in response to activation signalling pathway with e.g. prolactin.

Example 19:

Probes for detection of NFAT redistribution.

Useful for monitoring signalling pathways involving activation of NFAT, e.g. to identify compounds which modulate the activity of the pathway in living cells.

NFAT, an activator of transcription, is a component of signalling pathways which is involved in e.g. immune responses.

a) The human NFAT1 gene (GenBank Accession number: U43342) is amplified using PCR according to standard protocols with primers NFAT-top (SEQ ID NO:84) and NFAT-bottom/+stop (SEQ ID NO:86). The PCR product is digested with restriction enzymes Xho1 and EcoR1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Xho1 and EcoR1. This produces an EGFP-NFAT fusion (SEQ ID NO:130 &131) under the control of a CMV promoter.

b) The human NFAT gene (GenBank Accession number: U43342) is amplified using PCR according to standard protocols with primers NFAT-top (SEQ ID NO:84) and NFAT-bottom/-stop (SEQ ID NO:85). The PCR product is digested with restriction enzymes Xho1 and EcoR1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with Xho1 and EcoR1. This produces an NFAT-EGFP fusion (SEQ ID NO:132 &133) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. Jurkat, in which the EGFP-NFAT probe and/or the NFAT-EGFP probe should change its cellular distribution from cytoplasmic to nuclear within minutes in response to activation of the signalling pathway with e.g. antibodies to CD3epsilon.

Example 20:

Probes for detection of NFkappaB redistribution.

Useful for monitoring signalling pathways leading to activation of NFkappaB, e.g. to identify compounds which modulate the activity of the pathway in living cells.

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NFkappaB, an activator of transcription, is a component of signalling pathways which are responsive to a varity of inducers including cytokines, lymphokines, some immunosuppressive agents.

a) The human NFkappaB p65 subunit gene (GenBank Accession number: M62399) is amplified using PCR according to standard protocols with primers NFkappaB-top (SEQ ID NO:87) and NFkappaB-bottom/+stop (SEQ ID NO:89). The PCR product is digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Xho1 and BamH1. This produces an EGFP-NFkappaB fusion (SEQ ID NO:142 & 143) under the control of a CMV promoter.

b) The human NFkappaB p65 subunit gene (GenBank Accession number: M62399) is amplified using PCR according to standard protocols with primers NFkappaB-top (SEQ ID NO:87) and NFkappaB-bottom/-stop (SEQ ID NO:88). The PCR product is digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with Xho1 and BamH1. This produces an NFkappaB-EGFP fusion (SEQ ID NO:140 & 141) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. Jurkat, in which the EGFP-NFkappaB probe and/or the NFkappaB-EGFP probe should change its cellular distribution from cytoplasmic to nuclear in response to activation of the signalling pathway with e.g. TNFalpha.

Example 21:

Probe for detection of RhoA redistribution.

Useful for monitoring signalling pathways involving RhoA, e.g. to identify compounds which modulate the activity of the pathway in living cells.

RhoA, a small GTPase, is a component of many signalling pathways, e.g. LPA induced cytoskeletal rearrangements.

The human RhoA gene (GenBank Accession number: L25080) was amplified using PCR according to standard protocols with primers RhoA-top (SEQ ID NO:92) and RhoA-bottom/+stop (SEQ ID NO:93). The PCR product was digested with restriction enzymes

Hind3 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Hind3and BamH1. This produced an EGFP-RhoA fusion (SEQ ID NO:126 &127) under the control of a CMV promoter.

The resulting plasmid is transfected into a suitable cell line, e.g. Swiss3T3, in which the EGFP-RhoA probe should change its cellular distribution from a reasonably homogenous to a peripheral distribution within minutes of activation of the signalling pathway with e.g. LPA.

Example 22:

Probes for detection of PKB redistribution.

Useful for monitoring signalling pathways involving PKB e.g. to identify compounds which modulate the activity of the pathway in living cells.

PKB, a serine/threonine kinase, is a component in various signalling pathways, many of which are activated by growth factors.

a) The human PKB gene (GenBank Accession number: M63167) is amplified using PCR according to standard protocols with primers PKB-top (SEQ ID NO:36) and PKB-bottom/+stop (SEQ ID NO:80) . The PCR product is digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-C1 (Clontech, Palo Alto; GenBank Accession number U55763) digested with Xho1 and BamH1. This produces an EGFP-PKB fusion (SEQ ID NO:138 & 139) under the control of a CMV promoter.

b) The human PKB gene (GenBank Accession number: M63167) was amplified using PCR according to standard protocols with primers PKB-top (SEQ ID NO:36) and PKB-bottom/-stop (SEQ ID NO:37) . The PCR product was digested with restriction enzymes Xho1 and BamH1, and ligated into pEGFP-N1 (Clontech, Palo Alto; GenBank Accession number U55762) digested with Xho1 and BamH1. This produced a PKB-EGFP fusion (SEQ ID NO:70 &71) under the control of a CMV promoter.

The resulting plasmids are transfected into a suitable cell line, e.g. CHO expressing the human insulin receptor, in which the EGFP-PKB probe and/or the PKB-EGFP probe cycles between cytoplasmic and membrane locations during the activation-deactivation process following addition of insulin. The transition should be apparent within minutes.

BNSDOCID: <WO___9845704A2_I_>

REFERENCES:

Adams, S.R., Harootunian, A.T., Buechler, Y.J., Taylor, S.S. & Tsien, R.Y. (1991) Nature **349**, 694-697

Blobe, G.C., Stribling, D.S., Fabbro, D., Stabel, S & Hannun, Y.A. (1996) J. Biol. Chem. **271**, 15823-15830

Chalfie, M., Tu, Y., Euskirchen, G., Ward, W.W. & Prasher, D.C. (1994) Science **263**, 802-805

Cossette, L.J., Hoglinger, O., Mou, L.J. & Shen, S.H. (1997) Exp. Cell Res. **223**, 459-466

DeBernardi, M.A. & Brooker, G. (1996) Proc. Natl. Acad. Sci. USA **93**, 4577-4582

Farese, R.V.. (1992) Biochem. J. **288**, 319-323

Fulop Jr., T., Leblanc, C., Lacombe, G. & Dupuis, G. (1995) FEBS Lett. **375**, 69-74

Godson, C., Masliah, E., Balboa, M.A., Ellisman, M.H. & Insel, P.A. (1996) Biochem. Biophys. Acta **1313**, 63-71

Khalil, R.A., Lajoie, C., Resnick, M.S. & Morgan, K.G. (1992) American Physiol. Society **c**, 714-719

Sano, M., Kohno, M. & Iwanaga, M. (1995) Brain Res. **688**, 213-218

Bastiaens, P.I.H. & Jovin, T.M. (1996) Proc. Natl. Acad. Sci. USA **93**, 8407-8412

Schmidt, D.J., Ikebe, M., Kitamura, K., & Fay, F.S. (1997) FASEB J. **11**, 2924 (Abstract)

Sakai, N., Sasaki, K., Hasegawa, C., Ohkura, M., Suminka, K., Shirai, Y. & Saito, N. (1996) Soc. Neuroscience **22**, 69P (Abstract)

Sakai, N., Sakai, K. Hasegawa, C., Ohkura, M., Sumioka, ., Shirai, Y., & Naoaki, S. (1997) Japanese Journal of Pharmacology **73**, 69P (Abstract of a meeting held 22-23 March)

SEQUENCE LISTING

(1) GENERAL INFORMATION

(i) APPLICANT: NovoNordisk, BioImage

(ii) TITLE OF THE INVENTION: A Method of Detecting Cellular Translocation of Biologically Active Polypeptides Using Fluorescense Imaging

(iii) NUMBER OF SEQUENCES: 143

(iv) CORRESPONDENCE ADDRESS:
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(F) ZIP: 2860

(v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Diskette
(B) COMPUTER: IBM Compatible
(C) OPERATING SYSTEM: DOS
(D) SOFTWARE: FastSEQ for Windows Version 2.0

(viii) ATTORNEY/AGENT INFORMATION:
(A) NAME: , PV&P R
(B) REGISTRATION NUMBER:
(C) REFERENCE/DOCKET NUMBER:

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 53 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

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(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 53 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

BNSDOCID: <WO___9845704A2_I_>

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(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

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(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

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(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

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(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

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BNSDOCID: <WO___9845704A2_I_>

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(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

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(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 55 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

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(A) LENGTH: 30 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

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(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 29 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

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BNSDOCID: <WO___9845704A2_I_>

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(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

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(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

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(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
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(2) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 28 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

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(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 28 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

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(2) INFORMATION FOR SEQ ID NO:16:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 29 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

ATGGATCCTC AGGACTCCAT CTCTTCTTG 29

(2) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 28 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

GTCTCGAGCC ATCATGAGCA GAAGCAAG 28

(2) INFORMATION FOR SEQ ID NO:18:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

GTGGATCCCA CTGCTGCACC TGTGCTA 27

(2) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 28 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

BNSDOCID: <WO___9845704A2_I_>

GTGGATCCTC ACTGCTGCAC CTGTGCTA 28

(2) INFORMATION FOR SEQ ID NO:20:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 40 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

CGCGAATTCC GCCACCATGA GTGCTGAGGG GTACCAGTAC 40

(2) INFORMATION FOR SEQ ID NO:21:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 32 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

CGCGGATCCT GTCGCCTCTG CTGTGCATAT AC 32

(2) INFORMATION FOR SEQ ID NO:22:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 30 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(vi) ORIGINAL SOURCE:
(A) ORGANISM: p85-top-C

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

GGGAGATCTA TGAGTGCTGA GGGGTACCAG 30

(2) INFORMATION FOR SEQ ID NO:23:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 34 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

GGGCGGATCC TCATCGCCTC TGCTGTGCAT ATAC 34

(2) INFORMATION FOR SEQ ID NO:24:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 33 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

GTGAATTCGA CCATGTCGTC CATCTTGCCA TTC 33

(2) INFORMATION FOR SEQ ID NO:25:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 31 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

GTGGTACCCA TGACATGCTT GAGCAACGCA C 31

(2) INFORMATION FOR SEQ ID NO:26:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 32 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

GTGGTACCTT ATGACATGCT TGAGCAACGC AC 32

(2) INFORMATION FOR SEQ ID NO:27:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 31 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

GTGAATTCGT CAATGGAGCT GGAAAACATC G 31

(2) INFORMATION FOR SEQ ID NO:28:

(i) SEQUENCE CHARACTERISTICS:

BNSDOCID: <WO___9845704A2_I_>

(A) LENGTH: 30 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

GTGGATCCCT GCTGCTTCCG GTGGAGTTCG 30

(2) INFORMATION FOR SEQ ID NO:29:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 31 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

GTGGATCCCT AGCTGCTTCC GGTGGAGTTC G 31

(2) INFORMATION FOR SEQ ID NO:30:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 32 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

GTAGATCTAC CATGGCGGGC TGGATCCAGG CC 32

(2) INFORMATION FOR SEQ ID NO:31:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 31 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:

GTGGTACCCA TGAGAGGGAG CCTCTGGCAG A 31

(2) INFORMATION FOR SEQ ID NO:32:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 31 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:

GTGGTACCTC ATGAGAGGGA GCCTCTGGCA G 31

(2) INFORMATION FOR SEQ ID NO:33:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 33 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

GTGAATTCAA CCATGGACAA TATGTCTATT ACG 33

(2) INFORMATION FOR SEQ ID NO:34:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 31 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:

GTGGATCCCA GTCTAAAGGT TGTGGGTCTG C 31

(2) INFORMATION FOR SEQ ID NO:35:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 32 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:

GTGGATCCTC AGTCTAAAGG TTGTGGGTCT GC 32

(2) INFORMATION FOR SEQ ID NO:36:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

GTCTCGAGGC ACCATGAGCG ACGTGGC 27

(2) INFORMATION FOR SEQ ID NO:37:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

TGGGATCCGA GGCCGTGCTG CTGGCCG 27

(2) INFORMATION FOR SEQ ID NO:38:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1896 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...1891
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:

```
ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15

GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30

GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45

TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC     192
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60

CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG     240
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80

CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG     288
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95
```

```
CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG      336
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110

GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC      384
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125

ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC      432
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140

AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC      480
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160

GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC      528
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175

GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC      576
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190

CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG      624
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205

AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC      672
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220

GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC      720
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240

GGA CTC AGA TCT CGA GCT CAA GCT TCG AAT TCA ACC ATG GCG GCG GCG      768
Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Thr Met Ala Ala Ala
                245                 250                 255

GCG GCT CAG GGG GGC GGG GGC GGG GAG CCC CGT AGA ACC GAG GGG GTC      816
Ala Ala Gln Gly Gly Gly Gly Gly Glu Pro Arg Arg Thr Glu Gly Val
            260                 265                 270

GGC CCG GGG GTC CCG GGG GAG GTG GAG ATG GTG AAG GGG CAG CCG TTC      864
Gly Pro Gly Val Pro Gly Glu Val Glu Met Val Lys Gly Gln Pro Phe
        275                 280                 285

GAC GTG GGC CCG CGC TAC ACG CAG TTG CAG TAC ATC GGC GAG GGC GCG      912
Asp Val Gly Pro Arg Tyr Thr Gln Leu Gln Tyr Ile Gly Glu Gly Ala
    290                 295                 300

TAC GGC ATG GTC AGC TCG GCC TAT GAC CAC GTG CGC AAG ACT CGC GTG      960
Tyr Gly Met Val Ser Ser Ala Tyr Asp His Val Arg Lys Thr Arg Val
305                 310                 315                 320
```


BNSDOCID: <WO___9845704A2_I_>

GCC ATC AAG AAG ATC AGC CCC TTC GAA CAT CAG ACC TAC TGC CAG CGC 1008
Ala Ile Lys Lys Ile Ser Pro Phe Glu His Gln Thr Tyr Cys Gln Arg
325 330 335

ACG CTC CGG GAG ATC CAG ATC CTG CTG CGC TTC CGC CAT GAG AAT GTC 1056
Thr Leu Arg Glu Ile Gln Ile Leu Leu Arg Phe Arg His Glu Asn Val
340 345 350

ATC GGC ATC CGA GAC ATT CTG CGG GCG TCC ACC CTG GAA GCC ATG AGA 1104
Ile Gly Ile Arg Asp Ile Leu Arg Ala Ser Thr Leu Glu Ala Met Arg
355 360 365

GAT GTC TAC ATT GTG CAG GAC CTG ATG GAG ACT GAC CTG TAC AAG TTG 1152
Asp Val Tyr Ile Val Gln Asp Leu Met Glu Thr Asp Leu Tyr Lys Leu
370 375 380

CTG AAA AGC CAG CAG CTG AGC AAT GAC CAT ATC TGC TAC TTC CTC TAC 1200
Leu Lys Ser Gln Gln Leu Ser Asn Asp His Ile Cys Tyr Phe Leu Tyr
385 390 395 400

CAG ATC CTG CGG GGC CTC AAG TAC ATC CAC TCC GCC AAC GTG CTC CAC 1248
Gln Ile Leu Arg Gly Leu Lys Tyr Ile His Ser Ala Asn Val Leu His
405 410 415

CGA GAT CTA AAG CCC TCC AAC CTG CTC AGC AAC ACC ACC TGC GAC CTT 1296
Arg Asp Leu Lys Pro Ser Asn Leu Leu Ser Asn Thr Thr Cys Asp Leu
420 425 430

AAG ATT TGT GAT TTC GGC CTG GCC CGG ATT GCC GAT CCT GAG CAT GAC 1344
Lys Ile Cys Asp Phe Gly Leu Ala Arg Ile Ala Asp Pro Glu His Asp
435 440 445

CAC ACC GGC TTC CTG ACG GAG TAT GTG GCT ACG CGC TGG TAC CGG GCC 1392
His Thr Gly Phe Leu Thr Glu Tyr Val Ala Thr Arg Trp Tyr Arg Ala
450 455 460

CCA GAG ATC ATG CTG AAC TCC AAG GGC TAT ACC AAG TCC ATC GAC ATC 1440
Pro Glu Ile Met Leu Asn Ser Lys Gly Tyr Thr Lys Ser Ile Asp Ile
465 470 475 480

TGG TCT GTG GGC TGC ATT CTG GCT GAG ATG CTC TCT AAC CGG CCC ATC 1488
Trp Ser Val Gly Cys Ile Leu Ala Glu Met Leu Ser Asn Arg Pro Ile
485 490 495

TTC CCT GGC AAG CAC TAC CTG GAT CAG CTC AAC CAC ATT CTG GGC ATC 1536
Phe Pro Gly Lys His Tyr Leu Asp Gln Leu Asn His Ile Leu Gly Ile
500 505 510

CTG GGC TCC CCA TCC CAG GAG GAC CTG AAT TGT ATC ATC AAC ATG AAG 1584
Leu Gly Ser Pro Ser Gln Glu Asp Leu Asn Cys Ile Ile Asn Met Lys
515 520 525

GCC CGA AAC TAC CTA CAG TCT CTG CCC TCC AAG ACC AAG GTG GCT TGG 1632
Ala Arg Asn Tyr Leu Gln Ser Leu Pro Ser Lys Thr Lys Val Ala Trp
530 535 540

BNSDOCID: <WO___9845704A2_I_>

```
GCC AAG CTT TTC CCC AAG TCA GAC TCC AAA GCC CTT GAC CTG CTG GAC    1680
Ala Lys Leu Phe Pro Lys Ser Asp Ser Lys Ala Leu Asp Leu Leu Asp
545                 550                 555                 560

CGG ATG TTA ACC TTT AAC CCC AAT AAA CGG ATC ACA GTG GAG GAA GCG    1728
Arg Met Leu Thr Phe Asn Pro Asn Lys Arg Ile Thr Val Glu Glu Ala
                565                 570                 575

CTG GCT CAC CCC TAC CTG GAG CAG TAC TAT GAC CCG ACG GAT GAG CCA    1776
Leu Ala His Pro Tyr Leu Glu Gln Tyr Tyr Asp Pro Thr Asp Glu Pro
            580                 585                 590

GTG GCC GAG GAG CCC TTC ACC TTC GCC ATG GAG CTG GAT GAC CTA CCT    1824
Val Ala Glu Glu Pro Phe Thr Phe Ala Met Glu Leu Asp Asp Leu Pro
        595                 600                 605

AAG GAG CGG CTG AAG GAG CTC ATC TTC CAG GAG ACA GCA CGC TTC CAG    1872
Lys Glu Arg Leu Lys Glu Leu Ile Phe Gln Glu Thr Ala Arg Phe Gln
    610                 615                 620

CCC GGA GTG CTG GAG GCC C CCTAG                                    1896
Pro Gly Val Leu Glu Ala Pro
625                 630
```

(2) INFORMATION FOR SEQ ID NO:39:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 631 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:

```
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140
```

```
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240
Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Thr Met Ala Ala Ala
                245                 250                 255
Ala Ala Gln Gly Gly Gly Gly Gly Glu Pro Arg Arg Thr Glu Gly Val
            260                 265                 270
Gly Pro Gly Val Pro Gly Glu Val Glu Met Val Lys Gly Gln Pro Phe
        275                 280                 285
Asp Val Gly Pro Arg Tyr Thr Gln Leu Gln Tyr Ile Gly Glu Gly Ala
    290                 295                 300
Tyr Gly Met Val Ser Ser Ala Tyr Asp His Val Arg Lys Thr Arg Val
305                 310                 315                 320
Ala Ile Lys Lys Ile Ser Pro Phe Glu His Gln Thr Tyr Cys Gln Arg
                325                 330                 335
Thr Leu Arg Glu Ile Gln Ile Leu Leu Arg Phe Arg His Glu Asn Val
            340                 345                 350
Ile Gly Ile Arg Asp Ile Leu Arg Ala Ser Thr Leu Glu Ala Met Arg
        355                 360                 365
Asp Val Tyr Ile Val Gln Asp Leu Met Glu Thr Asp Leu Tyr Lys Leu
    370                 375                 380
Leu Lys Ser Gln Gln Leu Ser Asn Asp His Ile Cys Tyr Phe Leu Tyr
385                 390                 395                 400
Gln Ile Leu Arg Gly Leu Lys Tyr Ile His Ser Ala Asn Val Leu His
                405                 410                 415
Arg Asp Leu Lys Pro Ser Asn Leu Leu Ser Asn Thr Thr Cys Asp Leu
            420                 425                 430
Lys Ile Cys Asp Phe Gly Leu Ala Arg Ile Ala Asp Pro Glu His Asp
        435                 440                 445
His Thr Gly Phe Leu Thr Glu Tyr Val Ala Thr Arg Trp Tyr Arg Ala
    450                 455                 460
Pro Glu Ile Met Leu Asn Ser Lys Gly Tyr Thr Lys Ser Ile Asp Ile
465                 470                 475                 480
Trp Ser Val Gly Cys Ile Leu Ala Glu Met Leu Ser Asn Arg Pro Ile
                485                 490                 495
Phe Pro Gly Lys His Tyr Leu Asp Gln Leu Asn His Ile Leu Gly Ile
            500                 505                 510
Leu Gly Ser Pro Ser Gln Glu Asp Leu Asn Cys Ile Ile Asn Met Lys
        515                 520                 525
Ala Arg Asn Tyr Leu Gln Ser Leu Pro Ser Lys Thr Lys Val Ala Trp
    530                 535                 540
Ala Lys Leu Phe Pro Lys Ser Asp Ser Lys Ala Leu Asp Leu Leu Asp
545                 550                 555                 560
Arg Met Leu Thr Phe Asn Pro Asn Lys Arg Ile Thr Val Glu Glu Ala
                565                 570                 575
Leu Ala His Pro Tyr Leu Glu Gln Tyr Tyr Asp Pro Thr Asp Glu Pro
            580                 585                 590
```

```
Val Ala Glu Glu Pro Phe Thr Phe Ala Met Glu Leu Asp Asp Leu Pro
        595                 600                 605
Lys Glu Arg Leu Lys Glu Leu Ile Phe Gln Glu Thr Ala Arg Phe Gln
    610                 615                 620
Pro Gly Val Leu Glu Ala Pro
625                 630
```

(2) INFORMATION FOR SEQ ID NO:40:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1818 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...1815
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:

```
ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15

GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30

GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45

TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC     192
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60

CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG     240
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80

CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG     288
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95

CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG     336
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110

GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC     384
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125
```


BNSDOCID: <WO___9845704A2_I_>

```
ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC      432
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140

AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC      480
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160

GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC      528
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175

GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC      576
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190

CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG      624
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205

AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC      672
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220

GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC      720
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240

GGA CTC AGA TCT CGA GTA ACC ATG GCG GCG GCG GCG GCG GCG GGC CCG      768
Gly Leu Arg Ser Arg Val Thr Met Ala Ala Ala Ala Ala Ala Gly Pro
                245                 250                 255

GAG ATG GTC CGC GGG CAG GTG TTC GAC GTG GGG CCG CGC TAC ACT AAT      816
Glu Met Val Arg Gly Gln Val Phe Asp Val Gly Pro Arg Tyr Thr Asn
            260                 265                 270

CTC TCG TAC ATC GGA GAA GGC GCC TAC GGC ATG GTT TGT TCT GCT TAT      864
Leu Ser Tyr Ile Gly Glu Gly Ala Tyr Gly Met Val Cys Ser Ala Tyr
        275                 280                 285

GAT AAT CTC AAC AAA GTT CGA GTT GCT ATC AAG AAA ATC AGT CCT TTT      912
Asp Asn Leu Asn Lys Val Arg Val Ala Ile Lys Lys Ile Ser Pro Phe
    290                 295                 300

GAG CAC CAG ACC TAC TGT CAG AGA ACC CTG AGA GAG ATA AAA ATC CTA      960
Glu His Gln Thr Tyr Cys Gln Arg Thr Leu Arg Glu Ile Lys Ile Leu
305                 310                 315                 320

CTG CGC TTC AGA CAT GAG AAC ATC ATC GGC ATC AAT GAC ATC ATC CGG     1008
Leu Arg Phe Arg His Glu Asn Ile Ile Gly Ile Asn Asp Ile Ile Arg
                325                 330                 335

GCA CCA ACC ATT GAG CAG ATG AAA GAT GTA TAT ATA GTA CAG GAC CTC     1056
Ala Pro Thr Ile Glu Gln Met Lys Asp Val Tyr Ile Val Gln Asp Leu
            340                 345                 350
```


BNSDOCID: <WO___9845704A2_I_>

```
ATG GAG ACA GAT CTT TAC AAG CTC TTG AAG ACA CAG CAC CTC AGC AAT    1104
Met Glu Thr Asp Leu Tyr Lys Leu Leu Lys Thr Gln His Leu Ser Asn
        355                 360                 365

GAT CAT ATC TGC TAT TTT CTT TAT CAG ATC CTG AGA GGA TTA AAG TAT    1152
Asp His Ile Cys Tyr Phe Leu Tyr Gln Ile Leu Arg Gly Leu Lys Tyr
    370                 375                 380

ATA CAT TCA GCT AAT GTT CTG CAC CGT GAC CTC AAG CCT TCC AAC CTC    1200
Ile His Ser Ala Asn Val Leu His Arg Asp Leu Lys Pro Ser Asn Leu
385                 390                 395                 400

CTG CTG AAC ACC ACT TGT GAT CTC AAG ATC TGT GAC TTT GGC CTT GCC    1248
Leu Leu Asn Thr Thr Cys Asp Leu Lys Ile Cys Asp Phe Gly Leu Ala
                405                 410                 415

CGT GTT GCA GAT CCA GAC CAT GAT CAT ACA GGG TTC TTG ACA GAG TAT    1296
Arg Val Ala Asp Pro Asp His Asp His Thr Gly Phe Leu Thr Glu Tyr
            420                 425                 430

GTA GCC ACG CGT TGG TAC AGA GCT CCA GAA ATT ATG TTG AAT TCC AAG    1344
Val Ala Thr Arg Trp Tyr Arg Ala Pro Glu Ile Met Leu Asn Ser Lys
        435                 440                 445

GGT TAT ACC AAG TCC ATT GAT ATT TGG TCT GTG GGC TGC ATC CTG GCA    1392
Gly Tyr Thr Lys Ser Ile Asp Ile Trp Ser Val Gly Cys Ile Leu Ala
    450                 455                 460

GAG ATG CTA TCC AAC AGG CCT ATC TTC CCA GGA AAG CAT TAC CTT GAC    1440
Glu Met Leu Ser Asn Arg Pro Ile Phe Pro Gly Lys His Tyr Leu Asp
465                 470                 475                 480

CAG CTG AAT CAC ATC CTG GGT ATT CTT GGA TCT CCA TCA CAG GAA GAT    1488
Gln Leu Asn His Ile Leu Gly Ile Leu Gly Ser Pro Ser Gln Glu Asp
                485                 490                 495

CTG AAT TGT ATA ATA AAT TTA AAA GCT AGA AAC TAT TTG CTT TCT CTC    1536
Leu Asn Cys Ile Ile Asn Leu Lys Ala Arg Asn Tyr Leu Leu Ser Leu
            500                 505                 510

CCG CAC AAA AAT AAG GTG CCG TGG AAC AGG TTG TTC CCA AAC GCT GAC    1584
Pro His Lys Asn Lys Val Pro Trp Asn Arg Leu Phe Pro Asn Ala Asp
        515                 520                 525

TCC AAA GCT CTG GAT TTA CTG GAT AAA ATG TTG ACA TTT AAC CCT CAC    1632
Ser Lys Ala Leu Asp Leu Leu Asp Lys Met Leu Thr Phe Asn Pro His
    530                 535                 540

AAG AGG ATT GAA GTT GAA CAG GCT CTG GCC CAC CCG TAC CTG GAG CAG    1680
Lys Arg Ile Glu Val Glu Gln Ala Leu Ala His Pro Tyr Leu Glu Gln
545                 550                 555                 560

TAT TAT GAC CCA AGT GAT GAG CCC ATT GCT GAA GCA CCA TTC AAG TTT    1728
Tyr Tyr Asp Pro Ser Asp Glu Pro Ile Ala Glu Ala Pro Phe Lys Phe
                565                 570                 575
```

```
GAC ATG GAG CTG GAC GAC TTA CCT AAG GAG AAG CTC AAA GAA CTC ATT     1776
Asp Met Glu Leu Asp Asp Leu Pro Lys Glu Lys Leu Lys Glu Leu Ile
            580                 585                 590

TTT GAA GAG ACT GCT CGA TTC CAG CCA GGA TAC AGA TCT TAA             1818
Phe Glu Glu Thr Ala Arg Phe Gln Pro Gly Tyr Arg Ser
        595                 600                 605
```

(2) INFORMATION FOR SEQ ID NO:41:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 605 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:

```
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240
Gly Leu Arg Ser Arg Val Thr Met Ala Ala Ala Ala Ala Ala Gly Pro
                245                 250                 255
Glu Met Val Arg Gly Gln Val Phe Asp Val Gly Pro Arg Tyr Thr Asn
            260                 265                 270
```


BNSDOCID: <WO___9845704A2_I_>

```
Leu Ser Tyr Ile Gly Glu Gly Ala Tyr Gly Met Val Cys Ser Ala Tyr
        275                 280                 285
Asp Asn Leu Asn Lys Val Arg Val Ala Ile Lys Lys Ile Ser Pro Phe
    290                 295                 300
Glu His Gln Thr Tyr Cys Gln Arg Thr Leu Arg Glu Ile Lys Ile Leu
305                 310                 315                 320
Leu Arg Phe Arg His Glu Asn Ile Ile Gly Ile Asn Asp Ile Ile Arg
                325                 330                 335
Ala Pro Thr Ile Glu Gln Met Lys Asp Val Tyr Ile Val Gln Asp Leu
            340                 345                 350
Met Glu Thr Asp Leu Tyr Lys Leu Leu Lys Thr Gln His Leu Ser Asn
        355                 360                 365
Asp His Ile Cys Tyr Phe Leu Tyr Gln Ile Leu Arg Gly Leu Lys Tyr
    370                 375                 380
Ile His Ser Ala Asn Val Leu His Arg Asp Leu Lys Pro Ser Asn Leu
385                 390                 395                 400
Leu Leu Asn Thr Thr Cys Asp Leu Lys Ile Cys Asp Phe Gly Leu Ala
                405                 410                 415
Arg Val Ala Asp Pro Asp His Asp His Thr Gly Phe Leu Thr Glu Tyr
            420                 425                 430
Val Ala Thr Arg Trp Tyr Arg Ala Pro Glu Ile Met Leu Asn Ser Lys
        435                 440                 445
Gly Tyr Thr Lys Ser Ile Asp Ile Trp Ser Val Gly Cys Ile Leu Ala
    450                 455                 460
Glu Met Leu Ser Asn Arg Pro Ile Phe Pro Gly Lys His Tyr Leu Asp
465                 470                 475                 480
Gln Leu Asn His Ile Leu Gly Ile Leu Gly Ser Pro Ser Gln Glu Asp
                485                 490                 495
Leu Asn Cys Ile Ile Asn Leu Lys Ala Arg Asn Tyr Leu Leu Ser Leu
            500                 505                 510
Pro His Lys Asn Lys Val Pro Trp Asn Arg Leu Phe Pro Asn Ala Asp
        515                 520                 525
Ser Lys Ala Leu Asp Leu Leu Asp Lys Met Leu Thr Phe Asn Pro His
    530                 535                 540
Lys Arg Ile Glu Val Glu Gln Ala Leu Ala His Pro Tyr Leu Glu Gln
545                 550                 555                 560
Tyr Tyr Asp Pro Ser Asp Glu Pro Ile Ala Glu Ala Pro Phe Lys Phe
                565                 570                 575
Asp Met Glu Leu Asp Asp Leu Pro Lys Glu Lys Leu Lys Glu Leu Ile
            580                 585                 590
Phe Glu Glu Thr Ala Arg Phe Gln Pro Gly Tyr Arg Ser
        595                 600                 605
```

(2) INFORMATION FOR SEQ ID NO:42:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2529 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...2526

BNSDOCID: <WO__9845704A2_I_>

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:

```
ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15

GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30

GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45

TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC     192
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60

CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG     240
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80

CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG     288
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95

CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG     336
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110

GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC     384
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125

ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC     432
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140

AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC     480
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160

GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC     528
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175

GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC     576
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190

CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG     624
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205
```

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AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC    672
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220

GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC    720
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240

GGA CTC AGA TCT CGA GCT CAA GCT TCG AAT TCG TCA ATG GAG CTG GAA    768
Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Ser Met Glu Leu Glu
                245                 250                 255

AAC ATC GTG GCC AAC ACG GTC TTG CTG AAA GCC AGG GAA GGG GGC GGA    816
Asn Ile Val Ala Asn Thr Val Leu Leu Lys Ala Arg Glu Gly Gly Gly
            260                 265                 270

GGA AAG CGC AAA GGG AAA AGC AAG AAG TGG AAA GAA ATC CTG AAG TTC    864
Gly Lys Arg Lys Gly Lys Ser Lys Lys Trp Lys Glu Ile Leu Lys Phe
        275                 280                 285

CCT CAC ATT AGC CAG TGT GAA GAC CTC CGA AGG ACC ATA GAC AGA GAT    912
Pro His Ile Ser Gln Cys Glu Asp Leu Arg Arg Thr Ile Asp Arg Asp
    290                 295                 300

TAC TGC AGT TTA TGT GAC AAG CAG CCA ATC GGG AGG CTG CTT TTC CGG    960
Tyr Cys Ser Leu Cys Asp Lys Gln Pro Ile Gly Arg Leu Leu Phe Arg
305                 310                 315                 320

CAG TTT TGT GAA ACC AGG CCT GGG CTG GAG TGT TAC ATT CAG TTC CTG   1008
Gln Phe Cys Glu Thr Arg Pro Gly Leu Glu Cys Tyr Ile Gln Phe Leu
                325                 330                 335

GAC TCC GTG GCA GAA TAT GAA GTT ACT CCA GAT GAA AAA CTG GGA GAG   1056
Asp Ser Val Ala Glu Tyr Glu Val Thr Pro Asp Glu Lys Leu Gly Glu
            340                 345                 350

AAA GGG AAG GAA ATT ATG ACC AAG TAC CTC ACC CCA AAG TCC CCT GTT   1104
Lys Gly Lys Glu Ile Met Thr Lys Tyr Leu Thr Pro Lys Ser Pro Val
        355                 360                 365

TTC ATA GCC CAA GTT GGC CAA GAC CTG GTC TCC CAG ACG GAG GAG AAG   1152
Phe Ile Ala Gln Val Gly Gln Asp Leu Val Ser Gln Thr Glu Glu Lys
    370                 375                 380

CTC CTA CAG AAG CCG TGC AAA GAA CTC TTT TCT GCC TGT GCA CAG TCT   1200
Leu Leu Gln Lys Pro Cys Lys Glu Leu Phe Ser Ala Cys Ala Gln Ser
385                 390                 395                 400

GTC CAC GAG TAC CTG AGG GGA GAA CCA TTC CAC GAA TAT CTG GAC AGC   1248
Val His Glu Tyr Leu Arg Gly Glu Pro Phe His Glu Tyr Leu Asp Ser
                405                 410                 415

ATG TTT TTT GAC CGC TTT CTC CAG TGG AAG TGG TTG GAA AGG CAA CCG   1296
Met Phe Phe Asp Arg Phe Leu Gln Trp Lys Trp Leu Glu Arg Gln Pro
            420                 425                 430
```

```
GTG ACC AAA AAC ACT TTC AGG CAG TAT CGA GTG CTA GGA AAA GGG GGC    1344
Val Thr Lys Asn Thr Phe Arg Gln Tyr Arg Val Leu Gly Lys Gly Gly
        435                 440                 445

TTC GGG GAG GTC TGT GCC TGC CAG GTT CGG GCC ACG GGT AAA ATG TAT    1392
Phe Gly Glu Val Cys Ala Cys Gln Val Arg Ala Thr Gly Lys Met Tyr
    450                 455                 460

GCC TGC AAG CGC TTG GAG AAG AAG AGG ATC AAA AAG AGG AAA GGG GAG    1440
Ala Cys Lys Arg Leu Glu Lys Lys Arg Ile Lys Lys Arg Lys Gly Glu
465                 470                 475                 480

TCC ATG GCC CTC AAT GAG AAG CAG ATC CTC GAG AAG GTC AAC AGT CAG    1488
Ser Met Ala Leu Asn Glu Lys Gln Ile Leu Glu Lys Val Asn Ser Gln
                485                 490                 495

TTT GTG GTC AAC CTG GCC TAT GCC TAC GAG ACC AAG GAT GCA CTG TGC    1536
Phe Val Val Asn Leu Ala Tyr Ala Tyr Glu Thr Lys Asp Ala Leu Cys
            500                 505                 510

TTG GTC CTG ACC ATC ATG AAT GGG GGT GAC CTG AAG TTC CAC ATC TAC    1584
Leu Val Leu Thr Ile Met Asn Gly Gly Asp Leu Lys Phe His Ile Tyr
        515                 520                 525

AAC ATG GGC AAC CCT GGC TTC GAG GAG GAG CGG GCC TTG TTT TAT GCG    1632
Asn Met Gly Asn Pro Gly Phe Glu Glu Glu Arg Ala Leu Phe Tyr Ala
    530                 535                 540

GCA GAG ATC CTC TGC GGC TTA GAA GAC CTC CAC CGT GAG AAC ACC GTC    1680
Ala Glu Ile Leu Cys Gly Leu Glu Asp Leu His Arg Glu Asn Thr Val
545                 550                 555                 560

TAC CGA GAT CTG AAA CCT GAA AAC ATC CTG TTA GAT GAT TAT GGC CAC    1728
Tyr Arg Asp Leu Lys Pro Glu Asn Ile Leu Leu Asp Asp Tyr Gly His
                565                 570                 575

ATT AGG ATC TCA GAC CTG GGC TTG GCT GTG AAG ATC CCC GAG GGA GAC    1776
Ile Arg Ile Ser Asp Leu Gly Leu Ala Val Lys Ile Pro Glu Gly Asp
            580                 585                 590

CTG ATC CGC GGC CGG GTG GGC ACT GTT GGC TAC ATG GCC CCC GAA GTC    1824
Leu Ile Arg Gly Arg Val Gly Thr Val Gly Tyr Met Ala Pro Glu Val
        595                 600                 605

CTG AAC AAC CAG AGG TAC GGC CTG AGC CCC GAC TAC TGG GGC CTT GGC    1872
Leu Asn Asn Gln Arg Tyr Gly Leu Ser Pro Asp Tyr Trp Gly Leu Gly
    610                 615                 620

TGC CTC ATC TAT GAG ATG ATC GAG GGC CAG TCG CCG TTC CGC GGC CGT    1920
Cys Leu Ile Tyr Glu Met Ile Glu Gly Gln Ser Pro Phe Arg Gly Arg
625                 630                 635                 640

AAG GAG AAG GTG AAG CGG GAG GAG GTG GAC CGC CGG GTC CTG GAG ACG    1968
Lys Glu Lys Val Lys Arg Glu Glu Val Asp Arg Arg Val Leu Glu Thr
                645                 650                 655
```

```
GAG GAG GTG TAC TCC CAC AAG TTC TCC GAG GAG GCC AAG TCC ATC TGC    2016
Glu Glu Val Tyr Ser His Lys Phe Ser Glu Glu Ala Lys Ser Ile Cys
           660                 665                 670

AAG ATG CTG CTC ACG AAA GAT GCG AAG CAG AGG CTG GGC TGC CAG GAG    2064
Lys Met Leu Leu Thr Lys Asp Ala Lys Gln Arg Leu Gly Cys Gln Glu
       675                 680                 685

GAG GGG GCT GCA GAG GTC AAG AGA CAC CCC TTC TTC AGG AAC ATG AAC    2112
Glu Gly Ala Ala Glu Val Lys Arg His Pro Phe Phe Arg Asn Met Asn
   690                 695                 700

TTC AAG CGC TTA GAA GCC GGG ATG TTG GAC CCT CCC TTC GTT CCA GAC    2160
Phe Lys Arg Leu Glu Ala Gly Met Leu Asp Pro Pro Phe Val Pro Asp
705                 710                 715                 720

CCC CGC GCT GTG TAC TGT AAG GAC GTG CTG GAC ATC GAG CAG TTC TCC    2208
Pro Arg Ala Val Tyr Cys Lys Asp Val Leu Asp Ile Glu Gln Phe Ser
               725                 730                 735

ACT GTG AAG GGC GTC AAT CTG GAC CAC ACA GAC GAC GAC TTC TAC TCC    2256
Thr Val Lys Gly Val Asn Leu Asp His Thr Asp Asp Asp Phe Tyr Ser
           740                 745                 750

AAG TTC TCC ACG GGC TCT GTG TCC ATC CCA TGG CAA AAC GAG ATG ATA    2304
Lys Phe Ser Thr Gly Ser Val Ser Ile Pro Trp Gln Asn Glu Met Ile
       755                 760                 765

GAA ACA GAA TGC TTT AAG GAG CTG AAC GTG TTT GGA CCT AAT GGT ACC    2352
Glu Thr Glu Cys Phe Lys Glu Leu Asn Val Phe Gly Pro Asn Gly Thr
   770                 775                 780

CTC CCG CCA GAT CTG AAC AGA AAC CAC CCT CCG GAA CCG CCC AAG AAA    2400
Leu Pro Pro Asp Leu Asn Arg Asn His Pro Pro Glu Pro Pro Lys Lys
785                 790                 795                 800

GGG CTG CTC CAG AGA CTC TTC AAG CGG CAG CAT CAG AAC AAT TCC AAG    2448
Gly Leu Leu Gln Arg Leu Phe Lys Arg Gln His Gln Asn Asn Ser Lys
               805                 810                 815

AGT TCG CCC AGC TCC AAG ACC AGT TTT AAC CAC CAC ATA AAC TCA AAC    2496
Ser Ser Pro Ser Ser Lys Thr Ser Phe Asn His His Ile Asn Ser Asn
           820                 825                 830

CAT GTC AGC TCG AAC TCC ACC GGA AGC AGC TAG                        2529
His Val Ser Ser Asn Ser Thr Gly Ser Ser
       835                 840
```

(2) INFORMATION FOR SEQ ID NO:43:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 842 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

BNSDOCID: <WO__9845704A2_I_>

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:

```
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240
Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Ser Met Glu Leu Glu
                245                 250                 255
Asn Ile Val Ala Asn Thr Val Leu Leu Lys Ala Arg Glu Gly Gly Gly
            260                 265                 270
Gly Lys Arg Lys Gly Lys Ser Lys Lys Trp Lys Glu Ile Leu Lys Phe
        275                 280                 285
Pro His Ile Ser Gln Cys Glu Asp Leu Arg Arg Thr Ile Asp Arg Asp
    290                 295                 300
Tyr Cys Ser Leu Cys Asp Lys Gln Pro Ile Gly Arg Leu Leu Phe Arg
305                 310                 315                 320
Gln Phe Cys Glu Thr Arg Pro Gly Leu Glu Cys Tyr Ile Gln Phe Leu
                325                 330                 335
Asp Ser Val Ala Glu Tyr Glu Val Thr Pro Asp Glu Lys Leu Gly Glu
            340                 345                 350
Lys Gly Lys Glu Ile Met Thr Lys Tyr Leu Thr Pro Lys Ser Pro Val
        355                 360                 365
Phe Ile Ala Gln Val Gly Gln Asp Leu Val Ser Gln Thr Glu Glu Lys
    370                 375                 380
Leu Leu Gln Lys Pro Cys Lys Glu Leu Phe Ser Ala Cys Ala Gln Ser
385                 390                 395                 400
```

```
Val His Glu Tyr Leu Arg Gly Glu Pro Phe His Glu Tyr Leu Asp Ser
                405                 410                 415
Met Phe Phe Asp Arg Phe Leu Gln Trp Lys Trp Leu Glu Arg Gln Pro
            420                 425                 430
Val Thr Lys Asn Thr Phe Arg Gln Tyr Arg Val Leu Gly Lys Gly Gly
        435                 440                 445
Phe Gly Glu Val Cys Ala Cys Gln Val Arg Ala Thr Gly Lys Met Tyr
    450                 455                 460
Ala Cys Lys Arg Leu Glu Lys Lys Arg Ile Lys Lys Arg Lys Gly Glu
465                 470                 475                 480
Ser Met Ala Leu Asn Glu Lys Gln Ile Leu Glu Lys Val Asn Ser Gln
                485                 490                 495
Phe Val Val Asn Leu Ala Tyr Ala Tyr Glu Thr Lys Asp Ala Leu Cys
            500                 505                 510
Leu Val Leu Thr Ile Met Asn Gly Gly Asp Leu Lys Phe His Ile Tyr
        515                 520                 525
Asn Met Gly Asn Pro Gly Phe Glu Glu Glu Arg Ala Leu Phe Tyr Ala
    530                 535                 540
Ala Glu Ile Leu Cys Gly Leu Glu Asp Leu His Arg Glu Asn Thr Val
545                 550                 555                 560
Tyr Arg Asp Leu Lys Pro Glu Asn Ile Leu Leu Asp Asp Tyr Gly His
                565                 570                 575
Ile Arg Ile Ser Asp Leu Gly Leu Ala Val Lys Ile Pro Glu Gly Asp
            580                 585                 590
Leu Ile Arg Gly Arg Val Gly Thr Val Gly Tyr Met Ala Pro Glu Val
        595                 600                 605
Leu Asn Asn Gln Arg Tyr Gly Leu Ser Pro Asp Tyr Trp Gly Leu Gly
    610                 615                 620
Cys Leu Ile Tyr Glu Met Ile Glu Gly Gln Ser Pro Phe Arg Gly Arg
625                 630                 635                 640
Lys Glu Lys Val Lys Arg Glu Glu Val Asp Arg Arg Val Leu Glu Thr
                645                 650                 655
Glu Glu Val Tyr Ser His Lys Phe Ser Glu Glu Ala Lys Ser Ile Cys
            660                 665                 670
Lys Met Leu Leu Thr Lys Asp Ala Lys Gln Arg Leu Gly Cys Gln Glu
        675                 680                 685
Glu Gly Ala Ala Glu Val Lys Arg His Pro Phe Phe Arg Asn Met Asn
    690                 695                 700
Phe Lys Arg Leu Glu Ala Gly Met Leu Asp Pro Pro Phe Val Pro Asp
705                 710                 715                 720
Pro Arg Ala Val Tyr Cys Lys Asp Val Leu Asp Ile Glu Gln Phe Ser
                725                 730                 735
Thr Val Lys Gly Val Asn Leu Asp His Thr Asp Asp Asp Phe Tyr Ser
            740                 745                 750
Lys Phe Ser Thr Gly Ser Val Ser Ile Pro Trp Gln Asn Glu Met Ile
        755                 760                 765
Glu Thr Glu Cys Phe Lys Glu Leu Asn Val Phe Gly Pro Asn Gly Thr
    770                 775                 780
Leu Pro Pro Asp Leu Asn Arg Asn His Pro Pro Glu Pro Pro Lys Lys
785                 790                 795                 800
Gly Leu Leu Gln Arg Leu Phe Lys Arg Gln His Gln Asn Asn Ser Lys
                805                 810                 815
Ser Ser Pro Ser Ser Lys Thr Ser Phe Asn His His Ile Asn Ser Asn
            820                 825                 830
His Val Ser Ser Asn Ser Thr Gly Ser Ser
        835                 840
```

(2) INFORMATION FOR SEQ ID NO:44:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1902 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...1899
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:

```
ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15

GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30

GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45

TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC     192
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60

CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG     240
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80

CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG     288
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95

CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG     336
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110

GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC     384
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125

ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC     432
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140

AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC     480
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
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145                 150                 155                 160

GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC     528
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175

GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC     576
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190

CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG     624
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205

AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC     672
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220

GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC     720
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240

GGA CTC AGA TCT CGA GCT CGA GCC ATC ATG AGC AGA AGC AAG CGT GAC     768
Gly Leu Arg Ser Arg Ala Arg Ala Ile Met Ser Arg Ser Lys Arg Asp
                245                 250                 255

AAC AAT TTT TAT AGT GTA GAG ATT GGA GAT TCT ACA TTC ACA GTC CTG     816
Asn Asn Phe Tyr Ser Val Glu Ile Gly Asp Ser Thr Phe Thr Val Leu
            260                 265                 270

AAA CGA TAT CAG AAT TTA AAA CCT ATA GGC TCA GGA GCT CAA GGA ATA     864
Lys Arg Tyr Gln Asn Leu Lys Pro Ile Gly Ser Gly Ala Gln Gly Ile
        275                 280                 285

GTA TGC GCA GCT TAT GAT GCC ATT CTT GAA AGA AAT GTT GCA ATC AAG     912
Val Cys Ala Ala Tyr Asp Ala Ile Leu Glu Arg Asn Val Ala Ile Lys
    290                 295                 300

AAG CTA AGC CGA CCA TTT CAG AAT CAG ACT CAT GCC AAG CGG GCC TAC     960
Lys Leu Ser Arg Pro Phe Gln Asn Gln Thr His Ala Lys Arg Ala Tyr
305                 310                 315                 320

AGA GAG CTA GTT CTT ATG AAA TGT GTT AAT CAC AAA AAT ATA ATT GGC    1008
Arg Glu Leu Val Leu Met Lys Cys Val Asn His Lys Asn Ile Ile Gly
                325                 330                 335

CTT TTG AAT GTT TTC ACA CCA CAG AAA TCC CTA GAA GAA TTT CAA GAT    1056
Leu Leu Asn Val Phe Thr Pro Gln Lys Ser Leu Glu Glu Phe Gln Asp
            340                 345                 350

GTT TAC ATA GTC ATG GAG CTC ATG GAT GCA AAT CTT TGC CAA GTG ATT    1104
Val Tyr Ile Val Met Glu Leu Met Asp Ala Asn Leu Cys Gln Val Ile
        355                 360                 365

CAG ATG GAG CTA GAT CAT GAA AGA ATG TCC TAC CTT CTC TAT CAG ATG    1152
Gln Met Glu Leu Asp His Glu Arg Met Ser Tyr Leu Leu Tyr Gln Met
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370 375 380

CTG TGT GGA ATC AAG CAC CTT CAT TCT GCT GGA ATT ATT CAT CGG GAC 1200
Leu Cys Gly Ile Lys His Leu His Ser Ala Gly Ile Ile His Arg Asp
385 390 395 400

TTA AAG CCC AGT AAT ATA GTA GTA AAA TCT GAT TGC ACT TTG AAG ATT 1248
Leu Lys Pro Ser Asn Ile Val Val Lys Ser Asp Cys Thr Leu Lys Ile
405 410 415

CTT GAC TTC GGT CTG GCC AGG ACT GCA GGA ACG AGT TTT ATG ATG ACG 1296
Leu Asp Phe Gly Leu Ala Arg Thr Ala Gly Thr Ser Phe Met Met Thr
420 425 430

CCT TAT GTA GTG ACT CGC TAC TAC AGA GCA CCC GAG GTC ATC CTT GGC 1344
Pro Tyr Val Val Thr Arg Tyr Tyr Arg Ala Pro Glu Val Ile Leu Gly
435 440 445

ATG GGC TAC AAG GAA AAC GTG GAT TTA TGG TCT GTG GGG TGC ATT ATG 1392
Met Gly Tyr Lys Glu Asn Val Asp Leu Trp Ser Val Gly Cys Ile Met
450 455 460

GGA GAA ATG GTT TGC CAC AAA ATC CTC TTT CCA GGA AGG GAC TAT ATT 1440
Gly Glu Met Val Cys His Lys Ile Leu Phe Pro Gly Arg Asp Tyr Ile
465 470 475 480

GAT CAG TGG AAT AAA GTT ATT GAA CAG CTT GGA ACA CCA TGT CCT GAA 1488
Asp Gln Trp Asn Lys Val Ile Glu Gln Leu Gly Thr Pro Cys Pro Glu
485 490 495

TTC ATG AAG AAA CTG CAA CCA ACA GTA AGG ACT TAC GTT GAA AAC AGA 1536
Phe Met Lys Lys Leu Gln Pro Thr Val Arg Thr Tyr Val Glu Asn Arg
500 505 510

CCT AAA TAT GCT GGA TAT AGC TTT GAG AAA CTC TTC CCT GAT GTC CTT 1584
Pro Lys Tyr Ala Gly Tyr Ser Phe Glu Lys Leu Phe Pro Asp Val Leu
515 520 525

TTC CCA GCT GAC TCA GAA CAC AAC AAA CTT AAA GCC AGT CAG GCA AGG 1632
Phe Pro Ala Asp Ser Glu His Asn Lys Leu Lys Ala Ser Gln Ala Arg
530 535 540

GAT TTG TTA TCC AAA ATG CTG GTA ATA GAT GCA TCT AAA AGG ATC TCT 1680
Asp Leu Leu Ser Lys Met Leu Val Ile Asp Ala Ser Lys Arg Ile Ser
545 550 555 560

GTA GAT GAA GCT CTC CAA CAC CCG TAC ATC AAT GTC TGG TAT GAT CCT 1728
Val Asp Glu Ala Leu Gln His Pro Tyr Ile Asn Val Trp Tyr Asp Pro
565 570 575

TCT GAA GCA GAA GCT CCA CCA CCA AAG ATC CCT GAC AAG CAG TTA GAT 1776
Ser Glu Ala Glu Ala Pro Pro Pro Lys Ile Pro Asp Lys Gln Leu Asp
580 585 590

GAA AGG GAA CAC ACA ATA GAA GAG TGG AAA GAA TTG ATA TAT AAG GAA 1824
Glu Arg Glu His Thr Ile Glu Glu Trp Lys Glu Leu Ile Tyr Lys Glu

595 600 605

GTT ATG GAC TTG GAG GAG AGA ACC AAG AAT GGA GTT ATA CGG GGG CAG 1872
Val Met Asp Leu Glu Glu Arg Thr Lys Asn Gly Val Ile Arg Gly Gln
610 615 620

CCC TCT CCT TTA GCA CAG GTG CAG CAG TGA 1902
Pro Ser Pro Leu Ala Gln Val Gln Gln
625 630

(2) INFORMATION FOR SEQ ID NO:45:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 633 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:45:

Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
1 5 10 15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
20 25 30
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
35 40 45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
50 55 60
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65 70 75 80
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
85 90 95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
100 105 110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
115 120 125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
130 135 140
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145 150 155 160
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
165 170 175
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
180 185 190
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
195 200 205
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
210 215 220
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225 230 235 240
Gly Leu Arg Ser Arg Ala Arg Ala Ile Met Ser Arg Ser Lys Arg Asp
245 250 255

BNSDOCID: <WO__9845704A2_I_>

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Asn Asn Phe Tyr Ser Val Glu Ile Gly Asp Ser Thr Phe Thr Val Leu
            260                 265                 270
Lys Arg Tyr Gln Asn Leu Lys Pro Ile Gly Ser Gly Ala Gln Gly Ile
        275                 280                 285
Val Cys Ala Ala Tyr Asp Ala Ile Leu Glu Arg Asn Val Ala Ile Lys
    290                 295                 300
Lys Leu Ser Arg Pro Phe Gln Asn Gln Thr His Ala Lys Arg Ala Tyr
305                 310                 315                 320
Arg Glu Leu Val Leu Met Lys Cys Val Asn His Lys Asn Ile Ile Gly
                325                 330                 335
Leu Leu Asn Val Phe Thr Pro Gln Lys Ser Leu Glu Glu Phe Gln Asp
            340                 345                 350
Val Tyr Ile Val Met Glu Leu Met Asp Ala Asn Leu Cys Gln Val Ile
        355                 360                 365
Gln Met Glu Leu Asp His Glu Arg Met Ser Tyr Leu Leu Tyr Gln Met
    370                 375                 380
Leu Cys Gly Ile Lys His Leu His Ser Ala Gly Ile Ile His Arg Asp
385                 390                 395                 400
Leu Lys Pro Ser Asn Ile Val Val Lys Ser Asp Cys Thr Leu Lys Ile
                405                 410                 415
Leu Asp Phe Gly Leu Ala Arg Thr Ala Gly Thr Ser Phe Met Met Thr
            420                 425                 430
Pro Tyr Val Val Thr Arg Tyr Tyr Arg Ala Pro Glu Val Ile Leu Gly
        435                 440                 445
Met Gly Tyr Lys Glu Asn Val Asp Leu Trp Ser Val Gly Cys Ile Met
    450                 455                 460
Gly Glu Met Val Cys His Lys Ile Leu Phe Pro Gly Arg Asp Tyr Ile
465                 470                 475                 480
Asp Gln Trp Asn Lys Val Ile Glu Gln Leu Gly Thr Pro Cys Pro Glu
                485                 490                 495
Phe Met Lys Lys Leu Gln Pro Thr Val Arg Thr Tyr Val Glu Asn Arg
            500                 505                 510
Pro Lys Tyr Ala Gly Tyr Ser Phe Glu Lys Leu Phe Pro Asp Val Leu
        515                 520                 525
Phe Pro Ala Asp Ser Glu His Asn Lys Leu Lys Ala Ser Gln Ala Arg
    530                 535                 540
Asp Leu Leu Ser Lys Met Leu Val Ile Asp Ala Ser Lys Arg Ile Ser
545                 550                 555                 560
Val Asp Glu Ala Leu Gln His Pro Tyr Ile Asn Val Trp Tyr Asp Pro
                565                 570                 575
Ser Glu Ala Glu Ala Pro Pro Pro Lys Ile Pro Asp Lys Gln Leu Asp
            580                 585                 590
Glu Arg Glu His Thr Ile Glu Glu Trp Lys Glu Leu Ile Tyr Lys Glu
        595                 600                 605
Val Met Asp Leu Glu Glu Arg Thr Lys Asn Gly Val Ile Arg Gly Gln
    610                 615                 620
Pro Ser Pro Leu Ala Gln Val Gln Gln
625                 630
```

(2) INFORMATION FOR SEQ ID NO:46:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1824 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...1821
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:46:

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ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15

GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30

GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45

TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC     192
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60

CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG     240
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80

CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG     288
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95

CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG     336
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110

GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC     384
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125

ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC     432
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140

AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC     480
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160

GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC     528
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175

GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC     576
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
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180 185 190

CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG 624
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
195 200 205

AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC 672
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
210 215 220

GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC 720
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225 230 235 240

GGA CTC AGA TCT CGA GGG AAA ATG TCT CAG GAG AGG CCC ACG TTC TAC 768
Gly Leu Arg Ser Arg Gly Lys Met Ser Gln Glu Arg Pro Thr Phe Tyr
245 250 255

CGG CAG GAG CTG AAC AAG ACA ATC TGG GAG GTG CCC GAG CGT TAC CAG 816
Arg Gln Glu Leu Asn Lys Thr Ile Trp Glu Val Pro Glu Arg Tyr Gln
260 265 270

AAC CTG TCT CCA GTG GGC TCT GGC GCC TAT GGC TCT GTG TGT GCT GCT 864
Asn Leu Ser Pro Val Gly Ser Gly Ala Tyr Gly Ser Val Cys Ala Ala
275 280 285

TTT GAC ACA AAA ACG GGG TTA CGT GTG GCA GTG AAG AAG CTC TCC AGA 912
Phe Asp Thr Lys Thr Gly Leu Arg Val Ala Val Lys Lys Leu Ser Arg
290 295 300

CCA TTT CAG TCC ATC ATT CAT GCG AAA AGA ACC TAC AGA GAA CTG CGG 960
Pro Phe Gln Ser Ile Ile His Ala Lys Arg Thr Tyr Arg Glu Leu Arg
305 310 315 320

TTA CTT AAA CAT ATG AAA CAT GAA AAT GTG ATT GGT CTG TTG GAC GTT 1008
Leu Leu Lys His Met Lys His Glu Asn Val Ile Gly Leu Leu Asp Val
325 330 335

TTT ACA CCT GCA AGG TCT CTG GAG GAA TTC AAT GAT GTG TAT CTG GTG 1056
Phe Thr Pro Ala Arg Ser Leu Glu Glu Phe Asn Asp Val Tyr Leu Val
340 345 350

ACC CAT CTC ATG GGG GCA GAT CTG AAC AAC ATT GTG AAA TGT CAG AAG 1104
Thr His Leu Met Gly Ala Asp Leu Asn Asn Ile Val Lys Cys Gln Lys
355 360 365

CTT ACA GAT GAC CAT GTT CAG TTC CTT ATC TAC CAA ATT CTC CGA GGT 1152
Leu Thr Asp Asp His Val Gln Phe Leu Ile Tyr Gln Ile Leu Arg Gly
370 375 380

CTA AAG TAT ATA CAT TCA GCT GAC ATA ATT CAC AGG GAC CTA AAA CCT 1200
Leu Lys Tyr Ile His Ser Ala Asp Ile Ile His Arg Asp Leu Lys Pro
385 390 395 400

AGT AAT CTA GCT GTG AAT GAA GAC TGT GAG CTG AAG ATT CTG GAT TTT 1248
Ser Asn Leu Ala Val Asn Glu Asp Cys Glu Leu Lys Ile Leu Asp Phe

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                    405                 410                 415

GGA CTG GCT CGG CAC ACA GAT GAT GAA ATG ACA GGC TAC GTG GCC ACT    1296
Gly Leu Ala Arg His Thr Asp Asp Glu Met Thr Gly Tyr Val Ala Thr
            420                 425                 430

AGG TGG TAC AGG GCT CCT GAG ATC ATG CTG AAC TGG ATG CAT TAC AAC    1344
Arg Trp Tyr Arg Ala Pro Glu Ile Met Leu Asn Trp Met His Tyr Asn
        435                 440                 445

CAG ACA GTT GAT ATT TGG TCA GTG GGA TGC ATA ATG GCC GAG CTG TTG    1392
Gln Thr Val Asp Ile Trp Ser Val Gly Cys Ile Met Ala Glu Leu Leu
    450                 455                 460

ACT GGA AGA ACA TTG TTT CCT GGT ACA GAC CAT ATT GAT CAG TTG AAG    1440
Thr Gly Arg Thr Leu Phe Pro Gly Thr Asp His Ile Asp Gln Leu Lys
465                 470                 475                 480

CTC ATT TTA AGA CTC GTT GGA ACC CCA GGG GCT GAG CTT TTG AAG AAA    1488
Leu Ile Leu Arg Leu Val Gly Thr Pro Gly Ala Glu Leu Leu Lys Lys
                485                 490                 495

ATC TCC TCA GAG TCT GCA AGA AAC TAT ATT CAG TCT TTG ACT CAG ATG    1536
Ile Ser Ser Glu Ser Ala Arg Asn Tyr Ile Gln Ser Leu Thr Gln Met
            500                 505                 510

CCG AAG ATG AAC TTT GCG AAT GTA TTT ATT GGT GCC AAT CCC CTG GCT    1584
Pro Lys Met Asn Phe Ala Asn Val Phe Ile Gly Ala Asn Pro Leu Ala
        515                 520                 525

GTC GAC TTG CTG GAG AAG ATG CTT GTA TTG GAC TCA GAT AAG AGA ATT    1632
Val Asp Leu Leu Glu Lys Met Leu Val Leu Asp Ser Asp Lys Arg Ile
    530                 535                 540

ACA GCG GCC CAA GCC CTT GCA CAT GCC TAC TTT GCT CAG TAC CAC GAT    1680
Thr Ala Ala Gln Ala Leu Ala His Ala Tyr Phe Ala Gln Tyr His Asp
545                 550                 555                 560

CCT GAT GAT GAA CCA GTG GCC GAT CCT TAT GAT CAG TCC TTT GAA AGC    1728
Pro Asp Asp Glu Pro Val Ala Asp Pro Tyr Asp Gln Ser Phe Glu Ser
                565                 570                 575

AGG GAC CTC CTT ATA GAT GAG TGG AAA AGC CTG ACC TAT GAT GAA GTC    1776
Arg Asp Leu Leu Ile Asp Glu Trp Lys Ser Leu Thr Tyr Asp Glu Val
            580                 585                 590

ATC AGC TTT GTG CCA CCA CCC CTT GAC CAA GAA GAG ATG GAG TCC TGA     1824
Ile Ser Phe Val Pro Pro Pro Leu Asp Gln Glu Glu Met Glu Ser
        595                 600                 605
```

(2) INFORMATION FOR SEQ ID NO:47:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 607 amino acids
(B) TYPE: amino acid

(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:47:

```
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240
Gly Leu Arg Ser Arg Gly Lys Met Ser Gln Glu Arg Pro Thr Phe Tyr
                245                 250                 255
Arg Gln Glu Leu Asn Lys Thr Ile Trp Glu Val Pro Glu Arg Tyr Gln
            260                 265                 270
Asn Leu Ser Pro Val Gly Ser Gly Ala Tyr Gly Ser Val Cys Ala Ala
        275                 280                 285
Phe Asp Thr Lys Thr Gly Leu Arg Val Ala Val Lys Lys Leu Ser Arg
    290                 295                 300
Pro Phe Gln Ser Ile Ile His Ala Lys Arg Thr Tyr Arg Glu Leu Arg
305                 310                 315                 320
Leu Leu Lys His Met Lys His Glu Asn Val Ile Gly Leu Leu Asp Val
                325                 330                 335
Phe Thr Pro Ala Arg Ser Leu Glu Glu Phe Asn Asp Val Tyr Leu Val
            340                 345                 350
Thr His Leu Met Gly Ala Asp Leu Asn Asn Ile Val Lys Cys Gln Lys
        355                 360                 365
Leu Thr Asp Asp His Val Gln Phe Leu Ile Tyr Gln Ile Leu Arg Gly
    370                 375                 380
```

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Leu Lys Tyr Ile His Ser Ala Asp Ile Ile His Arg Asp Leu Lys Pro
385                 390                 395                 400
Ser Asn Leu Ala Val Asn Glu Asp Cys Glu Leu Lys Ile Leu Asp Phe
                405                 410                 415
Gly Leu Ala Arg His Thr Asp Asp Glu Met Thr Gly Tyr Val Ala Thr
            420                 425                 430
Arg Trp Tyr Arg Ala Pro Glu Ile Met Leu Asn Trp Met His Tyr Asn
        435                 440                 445
Gln Thr Val Asp Ile Trp Ser Val Gly Cys Ile Met Ala Glu Leu Leu
    450                 455                 460
Thr Gly Arg Thr Leu Phe Pro Gly Thr Asp His Ile Asp Gln Leu Lys
465                 470                 475                 480
Leu Ile Leu Arg Leu Val Gly Thr Pro Gly Ala Glu Leu Leu Lys Lys
                485                 490                 495
Ile Ser Ser Glu Ser Ala Arg Asn Tyr Ile Gln Ser Leu Thr Gln Met
            500                 505                 510
Pro Lys Met Asn Phe Ala Asn Val Phe Ile Gly Ala Asn Pro Leu Ala
        515                 520                 525
Val Asp Leu Leu Glu Lys Met Leu Val Leu Asp Ser Asp Lys Arg Ile
    530                 535                 540
Thr Ala Ala Gln Ala Leu Ala His Ala Tyr Phe Ala Gln Tyr His Asp
545                 550                 555                 560
Pro Asp Asp Glu Pro Val Ala Asp Pro Tyr Asp Gln Ser Phe Glu Ser
                565                 570                 575
Arg Asp Leu Leu Ile Asp Glu Trp Lys Ser Leu Thr Tyr Asp Glu Val
            580                 585                 590
Ile Ser Phe Val Pro Pro Pro Leu Asp Gln Glu Glu Met Glu Ser
        595                 600                 605
```

(2) INFORMATION FOR SEQ ID NO:48:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2907 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...2904
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:48:

```
ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15

GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30

GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
```

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                35                  40                  45

TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC      192
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60

CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG      240
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80

CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG      288
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95

CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG      336
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110

GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC      384
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125

ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC      432
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140

AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC      480
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160

GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC      528
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175

GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC      576
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190

CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG      624
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205

AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC      672
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220

GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC      720
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240

GGA CTC AGA TCT ATG AGT GCT GAG GGG TAC CAG TAC AGA GCG CTG TAT      768
Gly Leu Arg Ser Met Ser Ala Glu Gly Tyr Gln Tyr Arg Ala Leu Tyr
                245                 250                 255

GAT TAT AAA AAG GAA AGA GAA GAA GAT ATT GAC TTG CAC TTG GGT GAC      816
Asp Tyr Lys Lys Glu Arg Glu Glu Asp Ile Asp Leu His Leu Gly Asp
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                260                 265                 270

ATA TTG ACT GTG AAT AAA GGG TCC TTA GTA GCT CTT GGA TTC AGT GAT     864
Ile Leu Thr Val Asn Lys Gly Ser Leu Val Ala Leu Gly Phe Ser Asp
        275                 280                 285

GGA CAG GAA GCC AGG CCT GAA GAA ATT GGC TGG TTA AAT GGC TAT AAT     912
Gly Gln Glu Ala Arg Pro Glu Glu Ile Gly Trp Leu Asn Gly Tyr Asn
    290                 295                 300

GAA ACC ACA GGG GAA AGG GGG GAC TTT CCG GGA ACT TAC GTA GAA TAT     960
Glu Thr Thr Gly Glu Arg Gly Asp Phe Pro Gly Thr Tyr Val Glu Tyr
305                 310                 315                 320

ATT GGA AGG AAA AAA ATC TCG CCT CCC ACA CCA AAG CCC CGG CCA CCT    1008
Ile Gly Arg Lys Lys Ile Ser Pro Pro Thr Pro Lys Pro Arg Pro Pro
                325                 330                 335

CGG CCT CTT CCT GTT GCA CCA GGT TCT TCG AAA ACT GAA GCA GAT GTT    1056
Arg Pro Leu Pro Val Ala Pro Gly Ser Ser Lys Thr Glu Ala Asp Val
            340                 345                 350

GAA CAA CAA GCT TTG ACT CTC CCG GAT CTT GCA GAG CAG TTT GCC CCT    1104
Glu Gln Gln Ala Leu Thr Leu Pro Asp Leu Ala Glu Gln Phe Ala Pro
        355                 360                 365

CCT GAC ATT GCC CCG CCT CTT CTT ATC AAG CTC GTG GAA GCC ATT GAA    1152
Pro Asp Ile Ala Pro Pro Leu Leu Ile Lys Leu Val Glu Ala Ile Glu
    370                 375                 380

AAG AAA GGT CTG GAA TGT TCA ACT CTA TAC AGA ACA CAG AGC TCC AGC    1200
Lys Lys Gly Leu Glu Cys Ser Thr Leu Tyr Arg Thr Gln Ser Ser Ser
385                 390                 395                 400

AAC CTG GCA GAA TTA CGA CAG CTT CTT GAT TGT GAT ACA CCC TCC GTG    1248
Asn Leu Ala Glu Leu Arg Gln Leu Leu Asp Cys Asp Thr Pro Ser Val
                405                 410                 415

GAC TTG GAA ATG ATC GAT GTG CAC GTT TTG GCT GAC GCT TTC AAA CGC    1296
Asp Leu Glu Met Ile Asp Val His Val Leu Ala Asp Ala Phe Lys Arg
            420                 425                 430

TAT CTC CTG GAC TTA CCA AAT CCT GTC ATT CCA GCA GCC GTT TAC AGT    1344
Tyr Leu Leu Asp Leu Pro Asn Pro Val Ile Pro Ala Ala Val Tyr Ser
        435                 440                 445

GAA ATG ATT TCT TTA GCT CCA GAA GTA CAA AGC TCC GAA GAA TAT ATT    1392
Glu Met Ile Ser Leu Ala Pro Glu Val Gln Ser Ser Glu Glu Tyr Ile
    450                 455                 460

CAG CTA TTG AAG AAG CTT ATT AGG TCG CCT AGC ATA CCT CAT CAG TAT    1440
Gln Leu Leu Lys Lys Leu Ile Arg Ser Pro Ser Ile Pro His Gln Tyr
465                 470                 475                 480

TGG CTT ACG CTT CAG TAT TTG TTA AAA CAT TTC TTC AAG CTC TCT CAA    1488
Trp Leu Thr Leu Gln Tyr Leu Leu Lys His Phe Phe Lys Leu Ser Gln
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                    485                 490                 495

ACC TCC AGC AAA AAT CTG TTG AAT GCA AGA GTA CTC TCT GAA ATT TTC    1536
Thr Ser Ser Lys Asn Leu Leu Asn Ala Arg Val Leu Ser Glu Ile Phe
            500                 505                 510

AGC CCT ATG CTT TTC AGA TTC TCA GCA GCC AGC TCT GAT AAT ACT GAA    1584
Ser Pro Met Leu Phe Arg Phe Ser Ala Ala Ser Ser Asp Asn Thr Glu
        515                 520                 525

AAC CTC ATA AAA GTT ATA GAA ATT TTA ATC TCA ACT GAA TGG AAT GAA    1632
Asn Leu Ile Lys Val Ile Glu Ile Leu Ile Ser Thr Glu Trp Asn Glu
    530                 535                 540

CGA CAG CCT GCA CCA GCA CTG CCT CCT AAA CCA CCA AAA CCT ACT ACT    1680
Arg Gln Pro Ala Pro Ala Leu Pro Pro Lys Pro Pro Lys Pro Thr Thr
545                 550                 555                 560

GTA GCC AAC AAC GGT ATG AAT AAC AAT ATG TCC TTA CAA AAT GCT GAA    1728
Val Ala Asn Asn Gly Met Asn Asn Asn Met Ser Leu Gln Asn Ala Glu
                565                 570                 575

TGG TAC TGG GGA GAT ATC TCG AGG GAA GAA GTG AAT GAA AAA CTT CGA    1776
Trp Tyr Trp Gly Asp Ile Ser Arg Glu Glu Val Asn Glu Lys Leu Arg
            580                 585                 590

GAT ACA GCA GAC GGG ACC TTT TTG GTA CGA GAT GCG TCT ACT AAA ATG    1824
Asp Thr Ala Asp Gly Thr Phe Leu Val Arg Asp Ala Ser Thr Lys Met
        595                 600                 605

CAT GGT GAT TAT ACT CTT ACA CTA AGG AAA GGG GGA AAT AAC AAA TTA    1872
His Gly Asp Tyr Thr Leu Thr Leu Arg Lys Gly Gly Asn Asn Lys Leu
    610                 615                 620

ATC AAA ATA TTT CAT CGA GAT GGG AAA TAT GGC TTC TCT GAC CCA TTA    1920
Ile Lys Ile Phe His Arg Asp Gly Lys Tyr Gly Phe Ser Asp Pro Leu
625                 630                 635                 640

ACC TTC AGT TCT GTG GTT GAA TTA ATA AAC CAC TAC CGG AAT GAA TCT    1968
Thr Phe Ser Ser Val Val Glu Leu Ile Asn His Tyr Arg Asn Glu Ser
                645                 650                 655

CTA GCT CAG TAT AAT CCC AAA TTG GAT GTG AAA TTA CTT TAT CCA GTA    2016
Leu Ala Gln Tyr Asn Pro Lys Leu Asp Val Lys Leu Leu Tyr Pro Val
            660                 665                 670

TCC AAA TAC CAA CAG GAT CAA GTT GTC AAA GAA GAT AAT ATT GAA GCT    2064
Ser Lys Tyr Gln Gln Asp Gln Val Val Lys Glu Asp Asn Ile Glu Ala
        675                 680                 685

GTA GGG AAA AAA TTA CAT GAA TAT AAC ACT CAG TTT CAA GAA AAA AGT    2112
Val Gly Lys Lys Leu His Glu Tyr Asn Thr Gln Phe Gln Glu Lys Ser
    690                 695                 700

CGA GAA TAT GAT AGA TTA TAT GAA GAA TAT ACC CGC ACA TCC CAG GAA    2160
Arg Glu Tyr Asp Arg Leu Tyr Glu Glu Tyr Thr Arg Thr Ser Gln Glu
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705                 710                 715                 720

ATC CAA ATG AAA AGG ACA GCT ATT GAA GCA TTT AAT GAA ACC ATA AAA    2208
Ile Gln Met Lys Arg Thr Ala Ile Glu Ala Phe Asn Glu Thr Ile Lys
                725                 730                 735

ATA TTT GAA GAA CAG TGC CAG ACC CAA GAG CGG TAC AGC AAA GAA TAC    2256
Ile Phe Glu Glu Gln Cys Gln Thr Gln Glu Arg Tyr Ser Lys Glu Tyr
            740                 745                 750

ATA GAA AAG TTT AAA CGT GAA GGC AAT GAG AAA GAA ATA CAA AGG ATT    2304
Ile Glu Lys Phe Lys Arg Glu Gly Asn Glu Lys Glu Ile Gln Arg Ile
        755                 760                 765

ATG CAT AAT TAT GAT AAG TTG AAG TCT CGA ATC AGT GAA ATT ATT GAC    2352
Met His Asn Tyr Asp Lys Leu Lys Ser Arg Ile Ser Glu Ile Ile Asp
    770                 775                 780

AGT AGA AGA AGA TTG GAA GAA GAC TTG AAG AAG CAG GCA GCT GAG TAT    2400
Ser Arg Arg Arg Leu Glu Glu Asp Leu Lys Lys Gln Ala Ala Glu Tyr
785                 790                 795                 800

CGA GAA ATT GAC AAA CGT ATG AAC AGC ATT AAA CCA GAC CTT ATC CAG    2448
Arg Glu Ile Asp Lys Arg Met Asn Ser Ile Lys Pro Asp Leu Ile Gln
                805                 810                 815

CTG AGA AAG ACG AGA GAC CAA TAC TTG ATG TGG TTG ACT CAA AAA GGT    2496
Leu Arg Lys Thr Arg Asp Gln Tyr Leu Met Trp Leu Thr Gln Lys Gly
            820                 825                 830

GTT CGG CAA AAG AAG TTG AAC GAG TGG TTG GGC AAT GAA AAC ACT GAA    2544
Val Arg Gln Lys Lys Leu Asn Glu Trp Leu Gly Asn Glu Asn Thr Glu
        835                 840                 845

GAC CAA TAT TCA CTG GTG GAA GAT GAT GAA GAT TTG CCC CAT CAT GAT    2592
Asp Gln Tyr Ser Leu Val Glu Asp Asp Glu Asp Leu Pro His His Asp
    850                 855                 860

GAG AAG ACA TGG AAT GTT GGA AGC AGC AAC CGA AAC AAA GCT GAA AAC    2640
Glu Lys Thr Trp Asn Val Gly Ser Ser Asn Arg Asn Lys Ala Glu Asn
865                 870                 875                 880

CTG TTG CGA GGG AAG CGA GAT GGC ACT TTT CTT GTC CGG GAG AGC AGT    2688
Leu Leu Arg Gly Lys Arg Asp Gly Thr Phe Leu Val Arg Glu Ser Ser
                885                 890                 895

AAA CAG GGC TGC TAT GCC TGC TCT GTA GTG GTG GAC GGC GAA GTA AAG    2736
Lys Gln Gly Cys Tyr Ala Cys Ser Val Val Val Asp Gly Glu Val Lys
            900                 905                 910

CAT TGT GTC ATA AAC AAA ACA GCA ACT GGC TAT GGC TTT GCC GAG CCC    2784
His Cys Val Ile Asn Lys Thr Ala Thr Gly Tyr Gly Phe Ala Glu Pro
        915                 920                 925

TAT AAC TTG TAC AGC TCT CTG AAA GAA CTG GTG CTA CAT TAC CAA CAC    2832
Tyr Asn Leu Tyr Ser Ser Leu Lys Glu Leu Val Leu His Tyr Gln His
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930 935 940

ACC TCC CTT GTG CAG CAC AAC GAC TCC CTC AAT GTC ACA CTA GCC TAC 2880
Thr Ser Leu Val Gln His Asn Asp Ser Leu Asn Val Thr Leu Ala Tyr
945 950 955 960

CCA GTA TAT GCA CAG CAG AGG CGA TGA 2907
Pro Val Tyr Ala Gln Gln Arg Arg
965

(2) INFORMATION FOR SEQ ID NO:49:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 968 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:

Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
1 5 10 15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
20 25 30
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
35 40 45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
50 55 60
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65 70 75 80
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
85 90 95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
100 105 110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
115 120 125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
130 135 140
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145 150 155 160
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
165 170 175
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
180 185 190
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
195 200 205
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
210 215 220
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225 230 235 240
Gly Leu Arg Ser Met Ser Ala Glu Gly Tyr Gln Tyr Arg Ala Leu Tyr
245 250 255

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Asp Tyr Lys Lys Glu Arg Glu Glu Asp Ile Asp Leu His Leu Gly Asp
            260                 265                 270
Ile Leu Thr Val Asn Lys Gly Ser Leu Val Ala Leu Gly Phe Ser Asp
        275                 280                 285
Gly Gln Glu Ala Arg Pro Glu Glu Ile Gly Trp Leu Asn Gly Tyr Asn
    290                 295                 300
Glu Thr Thr Gly Glu Arg Gly Asp Phe Pro Gly Thr Tyr Val Glu Tyr
305                 310                 315                 320
Ile Gly Arg Lys Lys Ile Ser Pro Pro Thr Pro Lys Pro Arg Pro Pro
                325                 330                 335
Arg Pro Leu Pro Val Ala Pro Gly Ser Ser Lys Thr Glu Ala Asp Val
            340                 345                 350
Glu Gln Gln Ala Leu Thr Leu Pro Asp Leu Ala Glu Gln Phe Ala Pro
        355                 360                 365
Pro Asp Ile Ala Pro Pro Leu Leu Ile Lys Leu Val Glu Ala Ile Glu
    370                 375                 380
Lys Lys Gly Leu Glu Cys Ser Thr Leu Tyr Arg Thr Gln Ser Ser Ser
385                 390                 395                 400
Asn Leu Ala Glu Leu Arg Gln Leu Leu Asp Cys Asp Thr Pro Ser Val
                405                 410                 415
Asp Leu Glu Met Ile Asp Val His Val Leu Ala Asp Ala Phe Lys Arg
            420                 425                 430
Tyr Leu Leu Asp Leu Pro Asn Pro Val Ile Pro Ala Ala Val Tyr Ser
        435                 440                 445
Glu Met Ile Ser Leu Ala Pro Glu Val Gln Ser Ser Glu Glu Tyr Ile
    450                 455                 460
Gln Leu Leu Lys Lys Leu Ile Arg Ser Pro Ser Ile Pro His Gln Tyr
465                 470                 475                 480
Trp Leu Thr Leu Gln Tyr Leu Leu Lys His Phe Phe Lys Leu Ser Gln
                485                 490                 495
Thr Ser Ser Lys Asn Leu Leu Asn Ala Arg Val Leu Ser Glu Ile Phe
            500                 505                 510
Ser Pro Met Leu Phe Arg Phe Ser Ala Ala Ser Ser Asp Asn Thr Glu
        515                 520                 525
Asn Leu Ile Lys Val Ile Glu Ile Leu Ile Ser Thr Glu Trp Asn Glu
    530                 535                 540
Arg Gln Pro Ala Pro Ala Leu Pro Pro Lys Pro Pro Lys Pro Thr Thr
545                 550                 555                 560
Val Ala Asn Asn Gly Met Asn Asn Asn Met Ser Leu Gln Asn Ala Glu
                565                 570                 575
Trp Tyr Trp Gly Asp Ile Ser Arg Glu Glu Val Asn Glu Lys Leu Arg
            580                 585                 590
Asp Thr Ala Asp Gly Thr Phe Leu Val Arg Asp Ala Ser Thr Lys Met
        595                 600                 605
His Gly Asp Tyr Thr Leu Thr Leu Arg Lys Gly Gly Asn Asn Lys Leu
    610                 615                 620
Ile Lys Ile Phe His Arg Asp Gly Lys Tyr Gly Phe Ser Asp Pro Leu
625                 630                 635                 640
Thr Phe Ser Ser Val Val Glu Leu Ile Asn His Tyr Arg Asn Glu Ser
                645                 650                 655
Leu Ala Gln Tyr Asn Pro Lys Leu Asp Val Lys Leu Leu Tyr Pro Val
            660                 665                 670
Ser Lys Tyr Gln Gln Asp Gln Val Val Lys Glu Asp Asn Ile Glu Ala
        675                 680                 685
Val Gly Lys Lys Leu His Glu Tyr Asn Thr Gln Phe Gln Glu Lys Ser
    690                 695                 700
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Arg Glu Tyr Asp Arg Leu Tyr Glu Glu Tyr Thr Arg Thr Ser Gln Glu
705 710 715 720
Ile Gln Met Lys Arg Thr Ala Ile Glu Ala Phe Asn Glu Thr Ile Lys
725 730 735
Ile Phe Glu Glu Gln Cys Gln Thr Gln Glu Arg Tyr Ser Lys Glu Tyr
740 745 750
Ile Glu Lys Phe Lys Arg Glu Gly Asn Glu Lys Glu Ile Gln Arg Ile
755 760 765
Met His Asn Tyr Asp Lys Leu Lys Ser Arg Ile Ser Glu Ile Ile Asp
770 775 780
Ser Arg Arg Arg Leu Glu Glu Asp Leu Lys Lys Gln Ala Ala Glu Tyr
785 790 795 800
Arg Glu Ile Asp Lys Arg Met Asn Ser Ile Lys Pro Asp Leu Ile Gln
805 810 815
Leu Arg Lys Thr Arg Asp Gln Tyr Leu Met Trp Leu Thr Gln Lys Gly
820 825 830
Val Arg Gln Lys Lys Leu Asn Glu Trp Leu Gly Asn Glu Asn Thr Glu
835 840 845
Asp Gln Tyr Ser Leu Val Glu Asp Asp Glu Asp Leu Pro His His Asp
850 855 860
Glu Lys Thr Trp Asn Val Gly Ser Ser Asn Arg Asn Lys Ala Glu Asn
865 870 875 880
Leu Leu Arg Gly Lys Arg Asp Gly Thr Phe Leu Val Arg Glu Ser Ser
885 890 895
Lys Gln Gly Cys Tyr Ala Cys Ser Val Val Val Asp Gly Glu Val Lys
900 905 910
His Cys Val Ile Asn Lys Thr Ala Thr Gly Tyr Gly Phe Ala Glu Pro
915 920 925
Tyr Asn Leu Tyr Ser Ser Leu Lys Glu Leu Val Leu His Tyr Gln His
930 935 940
Thr Ser Leu Val Gln His Asn Asp Ser Leu Asn Val Thr Leu Ala Tyr
945 950 955 960
Pro Val Tyr Ala Gln Gln Arg Arg
965

(2) INFORMATION FOR SEQ ID NO:50:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2160 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...2157
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:50:

ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG 48
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
1 5 10 15

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GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30

GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45

TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC     192
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60

CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG     240
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80

CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG     288
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95

CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG     336
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110

GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC     384
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125

ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC     432
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140

AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC     480
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160

GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC     528
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175

GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC     576
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190

CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG     624
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205

AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC     672
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220

GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC     720
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240
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BNSDOCID: <WO___9845704A2_I_>

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GGA CTC AGA TCT CGA GCT CAA GCT TCG AAT TCG ACC ATG TCG TCC ATC      768
Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Thr Met Ser Ser Ile
                245                 250                 255

TTG CCA TTC ACG CCG CCA GTT GTG AAG AGA CTG CTG GGA TGG AAG AAG      816
Leu Pro Phe Thr Pro Pro Val Val Lys Arg Leu Leu Gly Trp Lys Lys
            260                 265                 270

TCA GCT GGT GGG TCT GGA GGA GCA GGC GGA GGA GAG CAG AAT GGG CAG      864
Ser Ala Gly Gly Ser Gly Gly Ala Gly Gly Gly Glu Gln Asn Gly Gln
        275                 280                 285

GAA GAA AAG TGG TGT GAG AAA GCA GTG AAA AGT CTG GTG AAG AAG CTA      912
Glu Glu Lys Trp Cys Glu Lys Ala Val Lys Ser Leu Val Lys Lys Leu
    290                 295                 300

AAG AAA ACA GGA CGA TTA GAT GAG CTT GAG AAA GCC ATC ACC ACT CAA      960
Lys Lys Thr Gly Arg Leu Asp Glu Leu Glu Lys Ala Ile Thr Thr Gln
305                 310                 315                 320

AAC TGT AAT ACT AAA TGT GTT ACC ATA CCA AGC ACT TGC TCT GAA ATT     1008
Asn Cys Asn Thr Lys Cys Val Thr Ile Pro Ser Thr Cys Ser Glu Ile
                325                 330                 335

TGG GGA CTG AGT ACA CCA AAT ACG ATA GAT CAG TGG GAT ACA ACA GGC     1056
Trp Gly Leu Ser Thr Pro Asn Thr Ile Asp Gln Trp Asp Thr Thr Gly
            340                 345                 350

CTT TAC AGC TTC TCT GAA CAA ACC AGG TCT CTT GAT GGT CGT CTC CAG     1104
Leu Tyr Ser Phe Ser Glu Gln Thr Arg Ser Leu Asp Gly Arg Leu Gln
        355                 360                 365

GTA TCC CAT CGA AAA GGA TTG CCA CAT GTT ATA TAT TGC CGA TTA TGG     1152
Val Ser His Arg Lys Gly Leu Pro His Val Ile Tyr Cys Arg Leu Trp
    370                 375                 380

CGC TGG CCT GAT CTT CAC AGT CAT CAT GAA CTC AAG GCA ATT GAA AAC     1200
Arg Trp Pro Asp Leu His Ser His His Glu Leu Lys Ala Ile Glu Asn
385                 390                 395                 400

TGC GAA TAT GCT TTT AAT CTT AAA AAG GAT GAA GTA TGT GTA AAC CCT     1248
Cys Glu Tyr Ala Phe Asn Leu Lys Lys Asp Glu Val Cys Val Asn Pro
                405                 410                 415

TAC CAC TAT CAG AGA GTT GAG ACA CCA GTT TTG CCT CCA GTA TTA GTG     1296
Tyr His Tyr Gln Arg Val Glu Thr Pro Val Leu Pro Pro Val Leu Val
            420                 425                 430

CCC CGA CAC ACC GAG ATC CTA ACA GAA CTT CCG CCT CTG GAT GAC TAT     1344
Pro Arg His Thr Glu Ile Leu Thr Glu Leu Pro Pro Leu Asp Asp Tyr
        435                 440                 445

ACT CAC TCC ATT CCA GAA AAC ACT AAC TTC CCA GCA GGA ATT GAG CCA     1392
Thr His Ser Ile Pro Glu Asn Thr Asn Phe Pro Ala Gly Ile Glu Pro
    450                 455                 460
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CAG AGT AAT TAT ATT CCA GAA ACG CCA CCT CCT GGA TAT ATC AGT GAA    1440
Gln Ser Asn Tyr Ile Pro Glu Thr Pro Pro Pro Gly Tyr Ile Ser Glu
465                 470                 475                 480

GAT GGA GAA ACA AGT GAC CAA CAG TTG AAT CAA AGT ATG GAC ACA GGC    1488
Asp Gly Glu Thr Ser Asp Gln Gln Leu Asn Gln Ser Met Asp Thr Gly
                485                 490                 495

TCT CCA GCA GAA CTA TCT CCT ACT ACT CTT TCC CCT GTT AAT CAT AGC    1536
Ser Pro Ala Glu Leu Ser Pro Thr Thr Leu Ser Pro Val Asn His Ser
            500                 505                 510

TTG GAT TTA CAG CCA GTT ACT TAC TCA GAA CCT GCA TTT TGG TGT TCA    1584
Leu Asp Leu Gln Pro Val Thr Tyr Ser Glu Pro Ala Phe Trp Cys Ser
        515                 520                 525

ATA GCA TAT TAT GAA TTA AAT CAG AGG GTT GGA GAA ACC TTC CAT GCA    1632
Ile Ala Tyr Tyr Glu Leu Asn Gln Arg Val Gly Glu Thr Phe His Ala
    530                 535                 540

TCA CAG CCC TCA CTC ACT GTA GAT GGC TTT ACA GAC CCA TCA AAT TCA    1680
Ser Gln Pro Ser Leu Thr Val Asp Gly Phe Thr Asp Pro Ser Asn Ser
545                 550                 555                 560

GAG AGG TTC TGC TTA GGT TTA CTC TCC AAT GTT AAC CGA AAT GCC ACG    1728
Glu Arg Phe Cys Leu Gly Leu Leu Ser Asn Val Asn Arg Asn Ala Thr
                565                 570                 575

GTA GAA ATG ACA AGA AGG CAT ATA GGA AGA GGA GTG CGC TTA TAC TAC    1776
Val Glu Met Thr Arg Arg His Ile Gly Arg Gly Val Arg Leu Tyr Tyr
            580                 585                 590

ATA GGT GGG GAA GTT TTT GCT GAG TGC CTA AGT GAT AGT GCA ATC TTT    1824
Ile Gly Gly Glu Val Phe Ala Glu Cys Leu Ser Asp Ser Ala Ile Phe
        595                 600                 605

GTG CAG AGC CCC AAT TGT AAT CAG AGA TAT GGC TGG CAC CCT GCA ACA    1872
Val Gln Ser Pro Asn Cys Asn Gln Arg Tyr Gly Trp His Pro Ala Thr
    610                 615                 620

GTG TGT AAA ATT CCA CCA GGC TGT AAT CTG AAG ATC TTC AAC AAC CAG    1920
Val Cys Lys Ile Pro Pro Gly Cys Asn Leu Lys Ile Phe Asn Asn Gln
625                 630                 635                 640

GAA TTT GCT GCT CTT CTG GCT CAG TCT GTT AAT CAG GGT TTT GAA GCC    1968
Glu Phe Ala Ala Leu Leu Ala Gln Ser Val Asn Gln Gly Phe Glu Ala
                645                 650                 655

GTC TAT CAG CTA ACT AGA ATG TGC ACC ATA AGA ATG AGT TTT GTG AAA    2016
Val Tyr Gln Leu Thr Arg Met Cys Thr Ile Arg Met Ser Phe Val Lys
            660                 665                 670

GGG TGG GGA GCA GAA TAC CGA AGG CAG ACG GTA ACA AGT ACT CCT TGC    2064
Gly Trp Gly Ala Glu Tyr Arg Arg Gln Thr Val Thr Ser Thr Pro Cys
        675                 680                 685
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TGG ATT GAA CTT CAT CTG AAT GGA CCT CTA CAG TGG TTG GAC AAA GTA     2112
Trp Ile Glu Leu His Leu Asn Gly Pro Leu Gln Trp Leu Asp Lys Val
    690                 695                 700

TTA ACT CAG ATG GGA TCC CCT TCA GTG CGT TGC TCA AGC ATG TCA TAA     2160
Leu Thr Gln Met Gly Ser Pro Ser Val Arg Cys Ser Ser Met Ser
705                 710                 715
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(2) INFORMATION FOR SEQ ID NO:51:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 719 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:

```
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240
Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Thr Met Ser Ser Ile
                245                 250                 255
Leu Pro Phe Thr Pro Pro Val Val Lys Arg Leu Leu Gly Trp Lys Lys
            260                 265                 270
```

```
Ser Ala Gly Gly Ser Gly Gly Ala Gly Gly Gly Glu Gln Asn Gly Gln
          275                 280                 285
Glu Glu Lys Trp Cys Glu Lys Ala Val Lys Ser Leu Val Lys Lys Leu
      290                 295                 300
Lys Lys Thr Gly Arg Leu Asp Glu Leu Glu Lys Ala Ile Thr Thr Gln
305                 310                 315                 320
Asn Cys Asn Thr Lys Cys Val Thr Ile Pro Ser Thr Cys Ser Glu Ile
                  325                 330                 335
Trp Gly Leu Ser Thr Pro Asn Thr Ile Asp Gln Trp Asp Thr Thr Gly
              340                 345                 350
Leu Tyr Ser Phe Ser Glu Gln Thr Arg Ser Leu Asp Gly Arg Leu Gln
          355                 360                 365
Val Ser His Arg Lys Gly Leu Pro His Val Ile Tyr Cys Arg Leu Trp
      370                 375                 380
Arg Trp Pro Asp Leu His Ser His His Glu Leu Lys Ala Ile Glu Asn
385                 390                 395                 400
Cys Glu Tyr Ala Phe Asn Leu Lys Lys Asp Glu Val Cys Val Asn Pro
                  405                 410                 415
Tyr His Tyr Gln Arg Val Glu Thr Pro Val Leu Pro Pro Val Leu Val
              420                 425                 430
Pro Arg His Thr Glu Ile Leu Thr Glu Leu Pro Pro Leu Asp Asp Tyr
          435                 440                 445
Thr His Ser Ile Pro Glu Asn Thr Asn Phe Pro Ala Gly Ile Glu Pro
      450                 455                 460
Gln Ser Asn Tyr Ile Pro Glu Thr Pro Pro Pro Gly Tyr Ile Ser Glu
465                 470                 475                 480
Asp Gly Glu Thr Ser Asp Gln Gln Leu Asn Gln Ser Met Asp Thr Gly
                  485                 490                 495
Ser Pro Ala Glu Leu Ser Pro Thr Thr Leu Ser Pro Val Asn His Ser
              500                 505                 510
Leu Asp Leu Gln Pro Val Thr Tyr Ser Glu Pro Ala Phe Trp Cys Ser
          515                 520                 525
Ile Ala Tyr Tyr Glu Leu Asn Gln Arg Val Gly Glu Thr Phe His Ala
      530                 535                 540
Ser Gln Pro Ser Leu Thr Val Asp Gly Phe Thr Asp Pro Ser Asn Ser
545                 550                 555                 560
Glu Arg Phe Cys Leu Gly Leu Leu Ser Asn Val Asn Arg Asn Ala Thr
                  565                 570                 575
Val Glu Met Thr Arg Arg His Ile Gly Arg Gly Val Arg Leu Tyr Tyr
              580                 585                 590
Ile Gly Gly Glu Val Phe Ala Glu Cys Leu Ser Asp Ser Ala Ile Phe
          595                 600                 605
Val Gln Ser Pro Asn Cys Asn Gln Arg Tyr Gly Trp His Pro Ala Thr
      610                 615                 620
Val Cys Lys Ile Pro Pro Gly Cys Asn Leu Lys Ile Phe Asn Asn Gln
625                 630                 635                 640
Glu Phe Ala Ala Leu Leu Ala Gln Ser Val Asn Gln Gly Phe Glu Ala
                  645                 650                 655
Val Tyr Gln Leu Thr Arg Met Cys Thr Ile Arg Met Ser Phe Val Lys
              660                 665                 670
Gly Trp Gly Ala Glu Tyr Arg Arg Gln Thr Val Thr Ser Thr Pro Cys
          675                 680                 685
Trp Ile Glu Leu His Leu Asn Gly Pro Leu Gln Trp Leu Asp Lys Val
      690                 695                 700
Leu Thr Gln Met Gly Ser Pro Ser Val Arg Cys Ser Ser Met Ser
705                 710                 715
```

(2) INFORMATION FOR SEQ ID NO:52:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2421 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...2418
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:

```
ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15

GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30

GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45

TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC     192
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60

CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG     240
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80

CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG     288
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95

CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG     336
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110

GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC     384
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125

ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC     432
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140

AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC     480
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
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145                 150                 155                 160

GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC      528
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175

GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC      576
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190

CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG      624
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205

AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC      672
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220

GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC      720
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240

GGA CTC AGA TCT CGA GCT CAA GCT TCG AAT TCG AAT TCA ACC ATG GAC      768
Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Asn Ser Thr Met Asp
                245                 250                 255

AAT ATG TCT ATT ACG AAT ACA CCA ACA AGT AAT GAT GCC TGT CTG AGC      816
Asn Met Ser Ile Thr Asn Thr Pro Thr Ser Asn Asp Ala Cys Leu Ser
            260                 265                 270

ATT GTG CAT AGT TTG ATG TGC CAT AGA CAA GGT GGA GAG AGT GAA ACA      864
Ile Val His Ser Leu Met Cys His Arg Gln Gly Gly Glu Ser Glu Thr
        275                 280                 285

TTT GCA AAA AGA GCA ATT GAA AGT TTG GTA AAG AAG CTG AAG GAG AAA      912
Phe Ala Lys Arg Ala Ile Glu Ser Leu Val Lys Lys Leu Lys Glu Lys
    290                 295                 300

AAA GAT GAA TTG GAT TCT TTA ATA ACA GCT ATA ACT ACA AAT GGA GCT      960
Lys Asp Glu Leu Asp Ser Leu Ile Thr Ala Ile Thr Thr Asn Gly Ala
305                 310                 315                 320

CAT CCT AGT AAA TGT GTT ACC ATA CAG AGA ACA TTG GAT GGG AGG CTT     1008
His Pro Ser Lys Cys Val Thr Ile Gln Arg Thr Leu Asp Gly Arg Leu
                325                 330                 335

CAG GTG GCT GGT CGG AAA GGA TTT CCT CAT GTG ATC TAT GCC CGT CTC     1056
Gln Val Ala Gly Arg Lys Gly Phe Pro His Val Ile Tyr Ala Arg Leu
            340                 345                 350

TGG AGG TGG CCT GAT CTT CAC AAA AAT GAA CTA AAA CAT GTT AAA TAT     1104
Trp Arg Trp Pro Asp Leu His Lys Asn Glu Leu Lys His Val Lys Tyr
        355                 360                 365

TGT CAG TAT GCG TTT GAC TTA AAA TGT GAT AGT GTC TGT GTG AAT CCA     1152
Cys Gln Tyr Ala Phe Asp Leu Lys Cys Asp Ser Val Cys Val Asn Pro
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370 375 380

TAT CAC TAC GAA CGA GTT GTA TCA CCT GGA ATT GAT CTC TCA GGA TTA 1200
Tyr His Tyr Glu Arg Val Val Ser Pro Gly Ile Asp Leu Ser Gly Leu
385 390 395 400

ACA CTG CAG AGT AAT GCT CCA TCA AGT ATG ATG GTG AAG GAT GAA TAT 1248
Thr Leu Gln Ser Asn Ala Pro Ser Ser Met Met Val Lys Asp Glu Tyr
405 410 415

GTG CAT GAC TTT GAG GGA CAG CCA TCG TTG TCC ACT GAA GGA CAT TCA 1296
Val His Asp Phe Glu Gly Gln Pro Ser Leu Ser Thr Glu Gly His Ser
420 425 430

ATT CAA ACC ATC CAG CAT CCA CCA AGT AAT CGT GCA TCG ACA GAG ACA 1344
Ile Gln Thr Ile Gln His Pro Pro Ser Asn Arg Ala Ser Thr Glu Thr
435 440 445

TAC AGC ACC CCA GCT CTG TTA GCC CCA TCT GAG TCT AAT GCT ACC AGC 1392
Tyr Ser Thr Pro Ala Leu Leu Ala Pro Ser Glu Ser Asn Ala Thr Ser
450 455 460

ACT GCC AAC TTT CCC AAC ATT CCT GTG GCT TCC ACA AGT CAG CCT GCC 1440
Thr Ala Asn Phe Pro Asn Ile Pro Val Ala Ser Thr Ser Gln Pro Ala
465 470 475 480

AGT ATA CTG GGG GGC AGC CAT AGT GAA GGA CTG TTG CAG ATA GCA TCA 1488
Ser Ile Leu Gly Gly Ser His Ser Glu Gly Leu Leu Gln Ile Ala Ser
485 490 495

GGG CCT CAG CCA GGA CAG CAG CAG AAT GGA TTT ACT GGT CAG CCA GCT 1536
Gly Pro Gln Pro Gly Gln Gln Gln Asn Gly Phe Thr Gly Gln Pro Ala
500 505 510

ACT TAC CAT CAT AAC AGC ACT ACC ACC TGG ACT GGA AGT AGG ACT GCA 1584
Thr Tyr His His Asn Ser Thr Thr Thr Trp Thr Gly Ser Arg Thr Ala
515 520 525

CCA TAC ACA CCT AAT TTG CCT CAC CAC CAA AAC GGC CAT CTT CAG CAC 1632
Pro Tyr Thr Pro Asn Leu Pro His His Gln Asn Gly His Leu Gln His
530 535 540

CAC CCG CCT ATG CCG CCC CAT CCC GGA CAT TAC TGG CCT GTT CAC AAT 1680
His Pro Pro Met Pro Pro His Pro Gly His Tyr Trp Pro Val His Asn
545 550 555 560

GAG CTT GCA TTC CAG CCT CCC ATT TCC AAT CAT CCT GCT CCT GAG TAT 1728
Glu Leu Ala Phe Gln Pro Pro Ile Ser Asn His Pro Ala Pro Glu Tyr
565 570 575

TGG TGT TCC ATT GCT TAC TTT GAA ATG GAT GTT CAG GTA GGA GAG ACA 1776
Trp Cys Ser Ile Ala Tyr Phe Glu Met Asp Val Gln Val Gly Glu Thr
580 585 590

TTT AAG GTT CCT TCA AGC TGC CCT ATT GTT ACT GTT GAT GGA TAC GTG 1824
Phe Lys Val Pro Ser Ser Cys Pro Ile Val Thr Val Asp Gly Tyr Val

```
          595                 600                 605

GAC CCT TCT GGA GGA GAT CGC TTT TGT TTG GGT CAA CTC TCC AAT GTC    1872
Asp Pro Ser Gly Gly Asp Arg Phe Cys Leu Gly Gln Leu Ser Asn Val
    610                 615                 620

CAC AGG ACA GAA GCC ATT GAG AGA GCA AGG TTG CAC ATA GGC AAA GGT    1920
His Arg Thr Glu Ala Ile Glu Arg Ala Arg Leu His Ile Gly Lys Gly
625                 630                 635                 640

GTG CAG TTG GAA TGT AAA GGT GAA GGT GAT GTT TGG GTC AGG TGC CTT    1968
Val Gln Leu Glu Cys Lys Gly Glu Gly Asp Val Trp Val Arg Cys Leu
                645                 650                 655

AGT GAC CAC GCG GTC TTT GTA CAG AGT TAC TAC TTA GAC AGA GAA GCT    2016
Ser Asp His Ala Val Phe Val Gln Ser Tyr Tyr Leu Asp Arg Glu Ala
            660                 665                 670

GGG CGT GCA CCT GGA GAT GCT GTT CAT AAG ATC TAC CCA AGT GCA TAT    2064
Gly Arg Ala Pro Gly Asp Ala Val His Lys Ile Tyr Pro Ser Ala Tyr
        675                 680                 685

ATA AAG GTC TTT GAT TTG CGT CAG TGT CAT CGA CAG ATG CAG CAG CAG    2112
Ile Lys Val Phe Asp Leu Arg Gln Cys His Arg Gln Met Gln Gln Gln
    690                 695                 700

GCG GCT ACT GCA CAA GCT GCA GCA GCT GCC CAG GCA GCA GCC GTG GCA    2160
Ala Ala Thr Ala Gln Ala Ala Ala Ala Ala Gln Ala Ala Ala Val Ala
705                 710                 715                 720

GGA AAC ATC CCT GGC CCA GGA TCA GTA GGT GGA ATA GCT CCA GCT ATC    2208
Gly Asn Ile Pro Gly Pro Gly Ser Val Gly Gly Ile Ala Pro Ala Ile
                725                 730                 735

AGT CTG TCA GCT GCT GCT GGA ATT GGT GTT GAT GAC CTT CGT CGC TTA    2256
Ser Leu Ser Ala Ala Ala Gly Ile Gly Val Asp Asp Leu Arg Arg Leu
            740                 745                 750

TGC ATA CTC AGG ATG AGT TTT GTG AAA GGC TGG GGA CCG GAT TAC CCA    2304
Cys Ile Leu Arg Met Ser Phe Val Lys Gly Trp Gly Pro Asp Tyr Pro
        755                 760                 765

AGA CAG AGC ATC AAA GAA ACA CCT TGC TGG ATT GAA ATT CAC TTA CAC    2352
Arg Gln Ser Ile Lys Glu Thr Pro Cys Trp Ile Glu Ile His Leu His
    770                 775                 780

CGG GCC CTC CAG CTC CTA GAC GAA GTA CTT CAT ACC ATG CCG ATT GCA    2400
Arg Ala Leu Gln Leu Leu Asp Glu Val Leu His Thr Met Pro Ile Ala
785                 790                 795                 800

GAC CCA CAA CCT TTA GAC TGA                                        2421
Asp Pro Gln Pro Leu Asp
                805
```

(2) INFORMATION FOR SEQ ID NO:53:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 806 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:

```
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240
Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Asn Ser Thr Met Asp
                245                 250                 255
Asn Met Ser Ile Thr Asn Thr Pro Thr Ser Asn Asp Ala Cys Leu Ser
            260                 265                 270
Ile Val His Ser Leu Met Cys His Arg Gln Gly Gly Glu Ser Glu Thr
        275                 280                 285
Phe Ala Lys Arg Ala Ile Glu Ser Leu Val Lys Lys Leu Lys Glu Lys
    290                 295                 300
Lys Asp Glu Leu Asp Ser Leu Ile Thr Ala Ile Thr Thr Asn Gly Ala
305                 310                 315                 320
His Pro Ser Lys Cys Val Thr Ile Gln Arg Thr Leu Asp Gly Arg Leu
                325                 330                 335
Gln Val Ala Gly Arg Lys Gly Phe Pro His Val Ile Tyr Ala Arg Leu
            340                 345                 350
```

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Trp Arg Trp Pro Asp Leu His Lys Asn Glu Leu Lys His Val Lys Tyr
        355                 360                 365
Cys Gln Tyr Ala Phe Asp Leu Lys Cys Asp Ser Val Cys Val Asn Pro
    370                 375                 380
Tyr His Tyr Glu Arg Val Val Ser Pro Gly Ile Asp Leu Ser Gly Leu
385                 390                 395                 400
Thr Leu Gln Ser Asn Ala Pro Ser Ser Met Met Val Lys Asp Glu Tyr
                405                 410                 415
Val His Asp Phe Glu Gly Gln Pro Ser Leu Ser Thr Glu Gly His Ser
            420                 425                 430
Ile Gln Thr Ile Gln His Pro Pro Ser Asn Arg Ala Ser Thr Glu Thr
        435                 440                 445
Tyr Ser Thr Pro Ala Leu Leu Ala Pro Ser Glu Ser Asn Ala Thr Ser
    450                 455                 460
Thr Ala Asn Phe Pro Asn Ile Pro Val Ala Ser Thr Ser Gln Pro Ala
465                 470                 475                 480
Ser Ile Leu Gly Gly Ser His Ser Glu Gly Leu Leu Gln Ile Ala Ser
                485                 490                 495
Gly Pro Gln Pro Gly Gln Gln Gln Asn Gly Phe Thr Gly Gln Pro Ala
            500                 505                 510
Thr Tyr His His Asn Ser Thr Thr Thr Trp Thr Gly Ser Arg Thr Ala
        515                 520                 525
Pro Tyr Thr Pro Asn Leu Pro His His Gln Asn Gly His Leu Gln His
    530                 535                 540
His Pro Pro Met Pro Pro His Pro Gly His Tyr Trp Pro Val His Asn
545                 550                 555                 560
Glu Leu Ala Phe Gln Pro Pro Ile Ser Asn His Pro Ala Pro Glu Tyr
                565                 570                 575
Trp Cys Ser Ile Ala Tyr Phe Glu Met Asp Val Gln Val Gly Glu Thr
            580                 585                 590
Phe Lys Val Pro Ser Ser Cys Pro Ile Val Thr Val Asp Gly Tyr Val
        595                 600                 605
Asp Pro Ser Gly Gly Asp Arg Phe Cys Leu Gly Gln Leu Ser Asn Val
    610                 615                 620
His Arg Thr Glu Ala Ile Glu Arg Ala Arg Leu His Ile Gly Lys Gly
625                 630                 635                 640
Val Gln Leu Glu Cys Lys Gly Glu Gly Asp Val Trp Val Arg Cys Leu
                645                 650                 655
Ser Asp His Ala Val Phe Val Gln Ser Tyr Tyr Leu Asp Arg Glu Ala
            660                 665                 670
Gly Arg Ala Pro Gly Asp Ala Val His Lys Ile Tyr Pro Ser Ala Tyr
        675                 680                 685
Ile Lys Val Phe Asp Leu Arg Gln Cys His Arg Gln Met Gln Gln Gln
    690                 695                 700
Ala Ala Thr Ala Gln Ala Ala Ala Ala Ala Gln Ala Ala Ala Val Ala
705                 710                 715                 720
Gly Asn Ile Pro Gly Pro Gly Ser Val Gly Gly Ile Ala Pro Ala Ile
                725                 730                 735
Ser Leu Ser Ala Ala Ala Gly Ile Gly Val Asp Asp Leu Arg Arg Leu
            740                 745                 750
Cys Ile Leu Arg Met Ser Phe Val Lys Gly Trp Gly Pro Asp Tyr Pro
        755                 760                 765
Arg Gln Ser Ile Lys Glu Thr Pro Cys Trp Ile Glu Ile His Leu His
    770                 775                 780
Arg Ala Leu Gln Leu Leu Asp Glu Val Leu His Thr Met Pro Ile Ala
785                 790                 795                 800
```

Asp Pro Gln Pro Leu Asp
805

(2) INFORMATION FOR SEQ ID NO:54:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3120 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...3117
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:

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ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15

GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30

GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45

TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC     192
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60

CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG     240
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80

CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG     288
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95

CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG     336
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110

GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC     384
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125

ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC     432
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140
```

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AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC     480
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160

GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC     528
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175

GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC     576
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190

CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG     624
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205

AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC     672
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220

GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC     720
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240

GGA CTC AGA TCT ACC ATG GCG GGC TGG ATC CAG GCC CAG CAG CTG CAG     768
Gly Leu Arg Ser Thr Met Ala Gly Trp Ile Gln Ala Gln Gln Leu Gln
                245                 250                 255

GGA GAC GCG CTG CGC CAG ATG CAG GTG CTG TAC GGC CAG CAC TTC CCC     816
Gly Asp Ala Leu Arg Gln Met Gln Val Leu Tyr Gly Gln His Phe Pro
            260                 265                 270

ATC GAG GTC CGG CAC TAC TTG GCC CAG TGG ATT GAG AGC CAG CCA TGG     864
Ile Glu Val Arg His Tyr Leu Ala Gln Trp Ile Glu Ser Gln Pro Trp
        275                 280                 285

GAT GCC ATT GAC TTG GAC AAT CCC CAG GAC AGA GCC CAA GCC ACC CAG     912
Asp Ala Ile Asp Leu Asp Asn Pro Gln Asp Arg Ala Gln Ala Thr Gln
    290                 295                 300

CTC CTG GAG GGC CTG GTG CAG GAG CTG CAG AAG AAG GCG GAG CAC CAG     960
Leu Leu Glu Gly Leu Val Gln Glu Leu Gln Lys Lys Ala Glu His Gln
305                 310                 315                 320

GTG GGG GAA GAT GGG TTT TTA CTG AAG ATC AAG CTG GGG CAC TAC GCC    1008
Val Gly Glu Asp Gly Phe Leu Leu Lys Ile Lys Leu Gly His Tyr Ala
                325                 330                 335

ACG CAG CTC CAG AAA ACA TAT GAC CGC TGC CCC CTG GAG CTG GTC CGC    1056
Thr Gln Leu Gln Lys Thr Tyr Asp Arg Cys Pro Leu Glu Leu Val Arg
            340                 345                 350

TGC ATC CGG CAC ATT CTG TAC AAT GAA CAG AGG CTG GTC CGA GAA GCC    1104
Cys Ile Arg His Ile Leu Tyr Asn Glu Gln Arg Leu Val Arg Glu Ala
        355                 360                 365
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BNSDOCID: <WO___9845704A2_I_>

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AAC AAT TGC AGC TCT CCG GCT GGG ATC CTG GTT GAC GCC ATG TCC CAG      1152
Asn Asn Cys Ser Ser Pro Ala Gly Ile Leu Val Asp Ala Met Ser Gln
    370                 375                 380

AAG CAC CTT CAG ATC AAC CAG ACA TTT GAG GAG CTG CGA CTG GTC ACG      1200
Lys His Leu Gln Ile Asn Gln Thr Phe Glu Glu Leu Arg Leu Val Thr
385                 390                 395                 400

CAG GAC ACA GAG AAT GAG CTG AAG AAA CTG CAG CAG ACT CAG GAG TAC      1248
Gln Asp Thr Glu Asn Glu Leu Lys Lys Leu Gln Gln Thr Gln Glu Tyr
                405                 410                 415

TTC ATC ATC CAG TAC CAG GAG AGC CTG AGG ATC CAA GCT CAG TTT GCC      1296
Phe Ile Ile Gln Tyr Gln Glu Ser Leu Arg Ile Gln Ala Gln Phe Ala
            420                 425                 430

CAG CTG GCC CAG CTG AGC CCC CAG GAG CGT CTG AGC CGG GAG ACG GCC      1344
Gln Leu Ala Gln Leu Ser Pro Gln Glu Arg Leu Ser Arg Glu Thr Ala
        435                 440                 445

CTC CAG CAG AAG CAG GTG TCT CTG GAG GCC TGG TTG CAG CGT GAG GCA      1392
Leu Gln Gln Lys Gln Val Ser Leu Glu Ala Trp Leu Gln Arg Glu Ala
    450                 455                 460

CAG ACA CTG CAG CAG TAC CGC GTG GAG CTG GCC GAG AAG CAC CAG AAG      1440
Gln Thr Leu Gln Gln Tyr Arg Val Glu Leu Ala Glu Lys His Gln Lys
465                 470                 475                 480

ACC CTG CAG CTG CTG CGG AAG CAG CAG ACC ATC ATC CTG GAT GAC GAG      1488
Thr Leu Gln Leu Leu Arg Lys Gln Gln Thr Ile Ile Leu Asp Asp Glu
                485                 490                 495

CTG ATC CAG TGG AAG CGG CGG CAG CAG CTG GCC GGG AAC GGC GGG CCC      1536
Leu Ile Gln Trp Lys Arg Arg Gln Gln Leu Ala Gly Asn Gly Gly Pro
            500                 505                 510

CCC GAG GGC AGC CTG GAC GTG CTA CAG TCC TGG TGT GAG AAG TTG GCC      1584
Pro Glu Gly Ser Leu Asp Val Leu Gln Ser Trp Cys Glu Lys Leu Ala
        515                 520                 525

GAG ATC ATC TGG CAG AAC CGG CAG CAG ATC CGC AGG GCT GAG CAC CTC      1632
Glu Ile Ile Trp Gln Asn Arg Gln Gln Ile Arg Arg Ala Glu His Leu
    530                 535                 540

TGC CAG CAG CTG CCC ATC CCC GGC CCA GTG GAG GAG ATG CTG GCC GAG      1680
Cys Gln Gln Leu Pro Ile Pro Gly Pro Val Glu Glu Met Leu Ala Glu
545                 550                 555                 560

GTC AAC GCC ACC ATC ACG GAC ATT ATC TCA GCC CTG GTG ACC AGC ACA      1728
Val Asn Ala Thr Ile Thr Asp Ile Ile Ser Ala Leu Val Thr Ser Thr
                565                 570                 575

TTC ATC ATT GAG AAG CAG CCT CCT CAG GTC CTG AAG ACC CAG ACC AAG      1776
Phe Ile Ile Glu Lys Gln Pro Pro Gln Val Leu Lys Thr Gln Thr Lys
            580                 585                 590
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TTT GCA GCC ACC GTA CGC CTG CTG GTG GGC GGG AAG CTG AAC GTG CAC   1824
Phe Ala Ala Thr Val Arg Leu Leu Val Gly Gly Lys Leu Asn Val His
        595                 600                 605

ATG AAT CCC CCC CAG GTG AAG GCC ACC ATC ATC AGT GAG CAG CAG GCC   1872
Met Asn Pro Pro Gln Val Lys Ala Thr Ile Ile Ser Glu Gln Gln Ala
    610                 615                 620

AAG TCT CTG CTT AAA AAT GAG AAC ACC CGC AAC GAG TGC AGT GGT GAG   1920
Lys Ser Leu Leu Lys Asn Glu Asn Thr Arg Asn Glu Cys Ser Gly Glu
625                 630                 635                 640

ATC CTG AAC AAC TGC TGC GTG ATG GAG TAC CAC CAA GCC ACG GGC ACC   1968
Ile Leu Asn Asn Cys Cys Val Met Glu Tyr His Gln Ala Thr Gly Thr
                645                 650                 655

CTC AGT GCC CAC TTC AGG AAC ATG TCA CTG AAG AGG ATC AAG CGT GCT   2016
Leu Ser Ala His Phe Arg Asn Met Ser Leu Lys Arg Ile Lys Arg Ala
            660                 665                 670

GAC CGG CGG GGT GCA GAG TCC GTG ACA GAG GAG AAG TTC ACA GTC CTG   2064
Asp Arg Arg Gly Ala Glu Ser Val Thr Glu Glu Lys Phe Thr Val Leu
        675                 680                 685

TTT GAG TCT CAG TTC AGT GTT GGC AGC AAT GAG CTT GTG TTC CAG GTG   2112
Phe Glu Ser Gln Phe Ser Val Gly Ser Asn Glu Leu Val Phe Gln Val
    690                 695                 700

AAG ACT CTG TCC CTA CCT GTG GTT GTC ATC GTC CAC GGC AGC CAG GAC   2160
Lys Thr Leu Ser Leu Pro Val Val Val Ile Val His Gly Ser Gln Asp
705                 710                 715                 720

CAC AAT GCC ACG GCT ACT GTG CTG TGG GAC AAT GCC TTT GCT GAG CCG   2208
His Asn Ala Thr Ala Thr Val Leu Trp Asp Asn Ala Phe Ala Glu Pro
                725                 730                 735

GGC AGG GTG CCA TTT GCC GTG CCT GAC AAA GTG CTG TGG CCG CAG CTG   2256
Gly Arg Val Pro Phe Ala Val Pro Asp Lys Val Leu Trp Pro Gln Leu
            740                 745                 750

TGT GAG GCG CTC AAC ATG AAA TTC AAG GCC GAA GTG CAG AGC AAC CGG   2304
Cys Glu Ala Leu Asn Met Lys Phe Lys Ala Glu Val Gln Ser Asn Arg
        755                 760                 765

GGC CTG ACC AAG GAG AAC CTC GTG TTC CTG GCG CAG AAA CTG TTC AAC   2352
Gly Leu Thr Lys Glu Asn Leu Val Phe Leu Ala Gln Lys Leu Phe Asn
    770                 775                 780

AAC AGC AGC AGC CAC CTG GAG GAC TAC AGT GGC CTG TCC GTG TCC TGG   2400
Asn Ser Ser Ser His Leu Glu Asp Tyr Ser Gly Leu Ser Val Ser Trp
785                 790                 795                 800

TCC CAG TTC AAC AGG GAG AAC TTG CCG GGC TGG AAC TAC ACC TTC TGG   2448
Ser Gln Phe Asn Arg Glu Asn Leu Pro Gly Trp Asn Tyr Thr Phe Trp
                805                 810                 815
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CAG TGG TTT GAC GGG GTG ATG GAG GTG TTG AAG AAG CAC CAC AAG CCC     2496
Gln Trp Phe Asp Gly Val Met Glu Val Leu Lys Lys His His Lys Pro
            820                 825                 830

CAC TGG AAT GAT GGG GCC ATC CTA GGT TTT GTG AAT AAG CAA CAG GCC     2544
His Trp Asn Asp Gly Ala Ile Leu Gly Phe Val Asn Lys Gln Gln Ala
        835                 840                 845

CAC GAC CTG CTC ATC AAC AAG CCC GAC GGG ACC TTC TTG TTG CGC TTT     2592
His Asp Leu Leu Ile Asn Lys Pro Asp Gly Thr Phe Leu Leu Arg Phe
    850                 855                 860

AGT GAC TCA GAA ATC GGG GGC ATC ACC ATC GCC TGG AAG TTT GAC TCC     2640
Ser Asp Ser Glu Ile Gly Gly Ile Thr Ile Ala Trp Lys Phe Asp Ser
865                 870                 875                 880

CCG GAA CGC AAC CTG TGG AAC CTG AAA CCA TTC ACC ACG CGG GAT TTC     2688
Pro Glu Arg Asn Leu Trp Asn Leu Lys Pro Phe Thr Thr Arg Asp Phe
                885                 890                 895

TCC ATC AGG TCC CTG GCT GAC CGG CTG GGG GAC CTG AGC TAT CTC ATC     2736
Ser Ile Arg Ser Leu Ala Asp Arg Leu Gly Asp Leu Ser Tyr Leu Ile
            900                 905                 910

TAT GTG TTT CCT GAC CGC CCC AAG GAT GAG GTC TTC TCC AAG TAC TAC     2784
Tyr Val Phe Pro Asp Arg Pro Lys Asp Glu Val Phe Ser Lys Tyr Tyr
        915                 920                 925

ACT CCT GTG CTG GCT AAA GCT GTT GAT GGA TAT GTG AAA CCA CAG ATC     2832
Thr Pro Val Leu Ala Lys Ala Val Asp Gly Tyr Val Lys Pro Gln Ile
    930                 935                 940

AAG CAA GTG GTC CCT GAG TTT GTG AAT GCA TCT GCA GAT GCT GGG GGC     2880
Lys Gln Val Val Pro Glu Phe Val Asn Ala Ser Ala Asp Ala Gly Gly
945                 950                 955                 960

AGC AGC GCC ACG TAC ATG GAC CAG GCC CCC TCC CCA GCT GTG TGC CCC     2928
Ser Ser Ala Thr Tyr Met Asp Gln Ala Pro Ser Pro Ala Val Cys Pro
                965                 970                 975

CAG GCT CCC TAT AAC ATG TAC CCA CAG AAC CCT GAC CAT GTA CTC GAT     2976
Gln Ala Pro Tyr Asn Met Tyr Pro Gln Asn Pro Asp His Val Leu Asp
            980                 985                 990

CAG GAT GGA GAA TTC GAC CTG GAT GAG ACC ATG GAT GTG GCC AGG CAC     3024
Gln Asp Gly Glu Phe Asp Leu Asp Glu Thr Met Asp Val Ala Arg His
        995                 1000                1005

GTG GAG GAA CTC TTA CGC CGA CCA ATG GAC AGT CTT GAC TCC CGC CTC     3072
Val Glu Glu Leu Leu Arg Arg Pro Met Asp Ser Leu Asp Ser Arg Leu
   1010                1015                1020

TCG CCC CCT GCC GGT CTT TTC ACC TCT GCC AGA GGC TCC CTC TCA TGA     3120
Ser Pro Pro Ala Gly Leu Phe Thr Ser Ala Arg Gly Ser Leu Ser
1025                1030                1035                1
```

(2) INFORMATION FOR SEQ ID NO:55:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1039 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:

```
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240
Gly Leu Arg Ser Thr Met Ala Gly Trp Ile Gln Ala Gln Gln Leu Gln
                245                 250                 255
Gly Asp Ala Leu Arg Gln Met Gln Val Leu Tyr Gly Gln His Phe Pro
            260                 265                 270
Ile Glu Val Arg His Tyr Leu Ala Gln Trp Ile Glu Ser Gln Pro Trp
        275                 280                 285
Asp Ala Ile Asp Leu Asp Asn Pro Gln Asp Arg Ala Gln Ala Thr Gln
    290                 295                 300
Leu Leu Glu Gly Leu Val Gln Glu Leu Gln Lys Lys Ala Glu His Gln
305                 310                 315                 320
Val Gly Glu Asp Gly Phe Leu Leu Lys Ile Lys Leu Gly His Tyr Ala
                325                 330                 335
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BNSDOCID: <WO___9845704A2_I_>

Thr Gln Leu Gln Lys Thr Tyr Asp Arg Cys Pro Leu Glu Leu Val Arg
340 345 350
Cys Ile Arg His Ile Leu Tyr Asn Glu Gln Arg Leu Val Arg Glu Ala
355 360 365
Asn Asn Cys Ser Ser Pro Ala Gly Ile Leu Val Asp Ala Met Ser Gln
370 375 380
Lys His Leu Gln Ile Asn Gln Thr Phe Glu Glu Leu Arg Leu Val Thr
385 390 395 400
Gln Asp Thr Glu Asn Glu Leu Lys Lys Leu Gln Gln Thr Gln Glu Tyr
405 410 415
Phe Ile Ile Gln Tyr Gln Glu Ser Leu Arg Ile Gln Ala Gln Phe Ala
420 425 430
Gln Leu Ala Gln Leu Ser Pro Gln Glu Arg Leu Ser Arg Glu Thr Ala
435 440 445
Leu Gln Gln Lys Gln Val Ser Leu Glu Ala Trp Leu Gln Arg Glu Ala
450 455 460
Gln Thr Leu Gln Gln Tyr Arg Val Glu Leu Ala Glu Lys His Gln Lys
465 470 475 480
Thr Leu Gln Leu Leu Arg Lys Gln Gln Thr Ile Ile Leu Asp Asp Glu
485 490 495
Leu Ile Gln Trp Lys Arg Arg Gln Gln Leu Ala Gly Asn Gly Gly Pro
500 505 510
Pro Glu Gly Ser Leu Asp Val Leu Gln Ser Trp Cys Glu Lys Leu Ala
515 520 525
Glu Ile Ile Trp Gln Asn Arg Gln Gln Ile Arg Arg Ala Glu His Leu
530 535 540
Cys Gln Gln Leu Pro Ile Pro Gly Pro Val Glu Glu Met Leu Ala Glu
545 550 555 560
Val Asn Ala Thr Ile Thr Asp Ile Ile Ser Ala Leu Val Thr Ser Thr
565 570 575
Phe Ile Ile Glu Lys Gln Pro Pro Gln Val Leu Lys Thr Gln Thr Lys
580 585 590
Phe Ala Ala Thr Val Arg Leu Leu Val Gly Gly Lys Leu Asn Val His
595 600 605
Met Asn Pro Pro Gln Val Lys Ala Thr Ile Ile Ser Glu Gln Gln Ala
610 615 620
Lys Ser Leu Leu Lys Asn Glu Asn Thr Arg Asn Glu Cys Ser Gly Glu
625 630 635 640
Ile Leu Asn Asn Cys Cys Val Met Glu Tyr His Gln Ala Thr Gly Thr
645 650 655
Leu Ser Ala His Phe Arg Asn Met Ser Leu Lys Arg Ile Lys Arg Ala
660 665 670
Asp Arg Arg Gly Ala Glu Ser Val Thr Glu Glu Lys Phe Thr Val Leu
675 680 685
Phe Glu Ser Gln Phe Ser Val Gly Ser Asn Glu Leu Val Phe Gln Val
690 695 700
Lys Thr Leu Ser Leu Pro Val Val Val Ile Val His Gly Ser Gln Asp
705 710 715 720
His Asn Ala Thr Ala Thr Val Leu Trp Asp Asn Ala Phe Ala Glu Pro
725 730 735
Gly Arg Val Pro Phe Ala Val Pro Asp Lys Val Leu Trp Pro Gln Leu
740 745 750
Cys Glu Ala Leu Asn Met Lys Phe Lys Ala Glu Val Gln Ser Asn Arg
755 760 765
Gly Leu Thr Lys Glu Asn Leu Val Phe Leu Ala Gln Lys Leu Phe Asn
770 775 780

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Asn Ser Ser Ser His Leu Glu Asp Tyr Ser Gly Leu Ser Val Ser Trp
785                 790                 795                 800
Ser Gln Phe Asn Arg Glu Asn Leu Pro Gly Trp Asn Tyr Thr Phe Trp
                805                 810                 815
Gln Trp Phe Asp Gly Val Met Glu Val Leu Lys Lys His His Lys Pro
            820                 825                 830
His Trp Asn Asp Gly Ala Ile Leu Gly Phe Val Asn Lys Gln Gln Ala
        835                 840                 845
His Asp Leu Leu Ile Asn Lys Pro Asp Gly Thr Phe Leu Leu Arg Phe
    850                 855                 860
Ser Asp Ser Glu Ile Gly Gly Ile Thr Ile Ala Trp Lys Phe Asp Ser
865                 870                 875                 880
Pro Glu Arg Asn Leu Trp Asn Leu Lys Pro Phe Thr Thr Arg Asp Phe
                885                 890                 895
Ser Ile Arg Ser Leu Ala Asp Arg Leu Gly Asp Leu Ser Tyr Leu Ile
            900                 905                 910
Tyr Val Phe Pro Asp Arg Pro Lys Asp Glu Val Phe Ser Lys Tyr Tyr
        915                 920                 925
Thr Pro Val Leu Ala Lys Ala Val Asp Gly Tyr Val Lys Pro Gln Ile
    930                 935                 940
Lys Gln Val Val Pro Glu Phe Val Asn Ala Ser Ala Asp Ala Gly Gly
945                 950                 955                 960
Ser Ser Ala Thr Tyr Met Asp Gln Ala Pro Ser Pro Ala Val Cys Pro
                965                 970                 975
Gln Ala Pro Tyr Asn Met Tyr Pro Gln Asn Pro Asp His Val Leu Asp
            980                 985                 990
Gln Asp Gly Glu Phe Asp Leu Asp Glu Thr Met Asp Val Ala Arg His
        995                1000                1005
Val Glu Glu Leu Leu Arg Arg Pro Met Asp Ser Leu Asp Ser Arg Leu
   1010                1015                1020
Ser Pro Pro Ala Gly Leu Phe Thr Ser Ala Arg Gly Ser Leu Ser
025                1030                1035                1
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(2) INFORMATION FOR SEQ ID NO:56:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1875 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...1872
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:

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ATG GCG GCG GCG GCG GCT CCG GGG GGC GGG GGC GGG GAG CCC AGG      48
Met Ala Ala Ala Ala Ala Pro Gly Gly Gly Gly Gly Glu Pro Arg
 1               5                  10                  15

GGA ACT GCT GGG GTC GTC CCG GTG GTC CCC GGG GAG GTG GAG GTG GTG      96
Gly Thr Ala Gly Val Val Pro Val Val Pro Gly Glu Val Glu Val Val
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                20                  25                  30

AAG GGG CAG CCA TTC GAT GTG GGC CCA CGC TAC ACG CAG CTG CAG TAC     144
Lys Gly Gln Pro Phe Asp Val Gly Pro Arg Tyr Thr Gln Leu Gln Tyr
        35                  40                  45

ATC GGC GAG GGC GCG TAC GGC ATG GTC AGC TCA GCT TAT GAC CAC GTG     192
Ile Gly Glu Gly Ala Tyr Gly Met Val Ser Ser Ala Tyr Asp His Val
    50                  55                  60

CGC AAG ACC AGA GTG GCC ATC AAG AAG ATC AGC CCC TTT GAG CAT CAA     240
Arg Lys Thr Arg Val Ala Ile Lys Lys Ile Ser Pro Phe Glu His Gln
65                  70                  75                  80

ACC TAC TGT CAG CGC ACG CTG AGG GAG ATC CAG ATC TTG CTG CGA TTC     288
Thr Tyr Cys Gln Arg Thr Leu Arg Glu Ile Gln Ile Leu Leu Arg Phe
                85                  90                  95

CGC CAT GAG AAT GTT ATA GGC ATC CGA GAC ATC CTC AGA GCG CCC ACC     336
Arg His Glu Asn Val Ile Gly Ile Arg Asp Ile Leu Arg Ala Pro Thr
            100                 105                 110

CTG GAA GCC ATG AGA GAT GTT TAC ATT GTT CAG GAC CTC ATG GAG ACA     384
Leu Glu Ala Met Arg Asp Val Tyr Ile Val Gln Asp Leu Met Glu Thr
        115                 120                 125

GAC CTG TAC AAG CTG CTT AAA AGC CAG CAG CTG AGC AAT GAC CAC ATC     432
Asp Leu Tyr Lys Leu Leu Lys Ser Gln Gln Leu Ser Asn Asp His Ile
    130                 135                 140

TGC TAC TTC CTC TAC CAG ATC CTC CGG GGC CTC AAG TAT ATA CAC TCA     480
Cys Tyr Phe Leu Tyr Gln Ile Leu Arg Gly Leu Lys Tyr Ile His Ser
145                 150                 155                 160

GCC AAT GTG CTG CAC CGG GAC CTG AAG CCT TCC AAT CTG CTT ATC AAC     528
Ala Asn Val Leu His Arg Asp Leu Lys Pro Ser Asn Leu Leu Ile Asn
                165                 170                 175

ACC ACC TGC GAC CTT AAG ATC TGT GAT TTT GGC CTG GCC CGG ATT GCT     576
Thr Thr Cys Asp Leu Lys Ile Cys Asp Phe Gly Leu Ala Arg Ile Ala
            180                 185                 190

GAC CCT GAG CAC GAC CAC ACT GGC TTT CTG ACG GAG TAT GTG GCC ACA     624
Asp Pro Glu His Asp His Thr Gly Phe Leu Thr Glu Tyr Val Ala Thr
        195                 200                 205

CGC TGG TAC CGA GCC CCA GAG ATC ATG CTT AAT TCC AAG GGC TAC ACC     672
Arg Trp Tyr Arg Ala Pro Glu Ile Met Leu Asn Ser Lys Gly Tyr Thr
    210                 215                 220

AAA TCC ATC GAC ATC TGG TCT GTG GGC TGC ATT CTG GCT GAG ATG CTC     720
Lys Ser Ile Asp Ile Trp Ser Val Gly Cys Ile Leu Ala Glu Met Leu
225                 230                 235                 240

TCC AAC CGG CCC ATC TTC CCC GGC AAG CAC TAC CTG GAC CAG CTC AAC     768
Ser Asn Arg Pro Ile Phe Pro Gly Lys His Tyr Leu Asp Gln Leu Asn
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                    245                 250                 255

CAC ATT CTA GGT ATC TTG GGT TCC CCA TCC CAG GAG GAC CTT AAT TGC     816
His Ile Leu Gly Ile Leu Gly Ser Pro Ser Gln Glu Asp Leu Asn Cys
                260                 265                 270

ATC ATT AAC ATG AAG GCC CGA AAC TAC CTG CAG TCT CTG CCC TCG AAA     864
Ile Ile Asn Met Lys Ala Arg Asn Tyr Leu Gln Ser Leu Pro Ser Lys
        275                 280                 285

ACC AAG GTG GCT TGG GCC AAG CTC TTT CCT AAA TCT GAC TCC AAA GCT     912
Thr Lys Val Ala Trp Ala Lys Leu Phe Pro Lys Ser Asp Ser Lys Ala
    290                 295                 300

CTT GAC CTG CTG GAC CGG ATG TTA ACC TTC AAC CCA AAC AAG CGC ATC     960
Leu Asp Leu Leu Asp Arg Met Leu Thr Phe Asn Pro Asn Lys Arg Ile
305                 310                 315                 320

ACA GTA GAG GAA GCG CTG GCT CAC CCT TAC CTG GAA CAG TAC TAC GAT    1008
Thr Val Glu Glu Ala Leu Ala His Pro Tyr Leu Glu Gln Tyr Tyr Asp
                325                 330                 335

CCG ACA GAT GAG CCA GTG GCC GAG GAG CCA TTC ACC TTC GAC ATG GAG    1056
Pro Thr Asp Glu Pro Val Ala Glu Glu Pro Phe Thr Phe Asp Met Glu
                340                 345                 350

CTG GAT GAC CTC CCC AAG GAG CGG CTG AAG GAG TTG ATC TTC CAG GAG    1104
Leu Asp Asp Leu Pro Lys Glu Arg Leu Lys Glu Leu Ile Phe Gln Glu
        355                 360                 365

ACA GCC CGC TTC CAG CCA GGG GCG CCA GAG GGC CCC GGG CGC GCC ATG    1152
Thr Ala Arg Phe Gln Pro Gly Ala Pro Glu Gly Pro Gly Arg Ala Met
    370                 375                 380

AGT AAA GGA GAA GAA CTT TTC ACT GGA GTT GTC CCA ATT CTT GTT GAA    1200
Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu
385                 390                 395                 400

TTA GAT GGC GAT GTT AAT GGG CAA AAA TTC TCT GTT AGT GGA GAG GGT    1248
Leu Asp Gly Asp Val Asn Gly Gln Lys Phe Ser Val Ser Gly Glu Gly
                405                 410                 415

GAA GGT GAT GCA ACA TAC GGA AAA CTT ACC CTT AAA TTT ATT TGC ACT    1296
Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr
                420                 425                 430

ACT GGG AAG CTA CCT GTT CCA TGG CCA ACG CTT GTC ACT ACT CTC ACT    1344
Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Thr
        435                 440                 445

TAT GGT GTT CAA TGC TTT TCT AGA TAC CCA GAT CAT ATG AAA CAG CAT    1392
Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln His
    450                 455                 460

GAC TTT TTC AAG AGT GCC ATG CCC GAA GGT TAT GTA CAG GAA AGA ACT    1440
Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr
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120

465 470 475 480

ATA TTT TAC AAA GAT GAC GGG AAC TAC AAG ACA CGT GCT GAA GTC AAG 1488
Ile Phe Tyr Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys
485 490 495

TTT GAA GGT GAT ACC CTT GTT AAT AGA ATC GAG TTA AAA GGT ATT GAT 1536
Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp
500 505 510

TTT AAA GAA GAT GGA AAC ATT CTT GGA CAC AAA ATG GAA TAC AAT TAT 1584
Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Met Glu Tyr Asn Tyr
515 520 525

AAC TCA CAT AAT GTA TAC ATC ATG GCA GAC AAA CCA AAG AAT GGC ATC 1632
Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Pro Lys Asn Gly Ile
530 535 540

AAA GTT AAC TTC AAA ATT AGA CAC AAC ATT AAA GAT GGA AGC GTT CAA 1680
Lys Val Asn Phe Lys Ile Arg His Asn Ile Lys Asp Gly Ser Val Gln
545 550 555 560

TTA GCA GAC CAT TAT CAA CAA AAT ACT CCA ATT GGC GAT GGC CCT GTC 1728
Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val
565 570 575

CTT TTA CCA GAC AAC CAT TAC CTG TCC ACG CAA TCT GCC CTT TCC AAA 1776
Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys
580 585 590

GAT CCC AAC GAA AAG AGA GAT CAC ATG ATC CTT CTT GAG TTT GTA ACA 1824
Asp Pro Asn Glu Lys Arg Asp His Met Ile Leu Leu Glu Phe Val Thr
595 600 605

GCT GCT GGG ATT ACA CAT GGC ATG GAT GAA CTA TAC AAA CCT CAG GAG T 1873
Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Lys Pro Gln Glu
610 615 620

AA 1875

(2) INFORMATION FOR SEQ ID NO:57:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 624 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:

Met Ala Ala Ala Ala Ala Ala Pro Gly Gly Gly Gly Gly Glu Pro Arg
1 5 10 15
Gly Thr Ala Gly Val Val Pro Val Val Pro Gly Glu Val Glu Val Val

120

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                20                  25                  30
Lys Gly Gln Pro Phe Asp Val Gly Pro Arg Tyr Thr Gln Leu Gln Tyr
        35                  40                  45
Ile Gly Glu Gly Ala Tyr Gly Met Val Ser Ser Ala Tyr Asp His Val
    50                  55                  60
Arg Lys Thr Arg Val Ala Ile Lys Lys Ile Ser Pro Phe Glu His Gln
65                  70                  75                  80
Thr Tyr Cys Gln Arg Thr Leu Arg Glu Ile Gln Ile Leu Leu Arg Phe
                85                  90                  95
Arg His Glu Asn Val Ile Gly Ile Arg Asp Ile Leu Arg Ala Pro Thr
            100                 105                 110
Leu Glu Ala Met Arg Asp Val Tyr Ile Val Gln Asp Leu Met Glu Thr
        115                 120                 125
Asp Leu Tyr Lys Leu Leu Lys Ser Gln Gln Leu Ser Asn Asp His Ile
    130                 135                 140
Cys Tyr Phe Leu Tyr Gln Ile Leu Arg Gly Leu Lys Tyr Ile His Ser
145                 150                 155                 160
Ala Asn Val Leu His Arg Asp Leu Lys Pro Ser Asn Leu Leu Ile Asn
                165                 170                 175
Thr Thr Cys Asp Leu Lys Ile Cys Asp Phe Gly Leu Ala Arg Ile Ala
            180                 185                 190
Asp Pro Glu His Asp His Thr Gly Phe Leu Thr Glu Tyr Val Ala Thr
        195                 200                 205
Arg Trp Tyr Arg Ala Pro Glu Ile Met Leu Asn Ser Lys Gly Tyr Thr
    210                 215                 220
Lys Ser Ile Asp Ile Trp Ser Val Gly Cys Ile Leu Ala Glu Met Leu
225                 230                 235                 240
Ser Asn Arg Pro Ile Phe Pro Gly Lys His Tyr Leu Asp Gln Leu Asn
                245                 250                 255
His Ile Leu Gly Ile Leu Gly Ser Pro Ser Gln Glu Asp Leu Asn Cys
            260                 265                 270
Ile Ile Asn Met Lys Ala Arg Asn Tyr Leu Gln Ser Leu Pro Ser Lys
        275                 280                 285
Thr Lys Val Ala Trp Ala Lys Leu Phe Pro Lys Ser Asp Ser Lys Ala
    290                 295                 300
Leu Asp Leu Leu Asp Arg Met Leu Thr Phe Asn Pro Asn Lys Arg Ile
305                 310                 315                 320
Thr Val Glu Glu Ala Leu Ala His Pro Tyr Leu Glu Gln Tyr Tyr Asp
                325                 330                 335
Pro Thr Asp Glu Pro Val Ala Glu Glu Pro Phe Thr Phe Asp Met Glu
            340                 345                 350
Leu Asp Asp Leu Pro Lys Glu Arg Leu Lys Glu Leu Ile Phe Gln Glu
        355                 360                 365
Thr Ala Arg Phe Gln Pro Gly Ala Pro Glu Gly Pro Gly Arg Ala Met
    370                 375                 380
Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu
385                 390                 395                 400
Leu Asp Gly Asp Val Asn Gly Gln Lys Phe Ser Val Ser Gly Glu Gly
                405                 410                 415
Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr
            420                 425                 430
Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Thr
        435                 440                 445
Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln His
    450                 455                 460
Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr
```

```
465                 470                 475                 480
Ile Phe Tyr Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys
                485                 490                 495
Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp
            500                 505                 510
Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Met Glu Tyr Asn Tyr
        515                 520                 525
Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Pro Lys Asn Gly Ile
    530                 535                 540
Lys Val Asn Phe Lys Ile Arg His Asn Ile Lys Asp Gly Ser Val Gln
545                 550                 555                 560
Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val
                565                 570                 575
Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys
            580                 585                 590
Asp Pro Asn Glu Lys Arg Asp His Met Ile Leu Leu Glu Phe Val Thr
        595                 600                 605
Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Lys Pro Gln Glu
    610                 615                 620
```

(2) INFORMATION FOR SEQ ID NO:58:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1815 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...1811
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:

```
ATG GCG GCG GCG GCG GCG GCG GGC CCG GAG ATG GTC CGC GGG CAG GTG      48
Met Ala Ala Ala Ala Ala Ala Gly Pro Glu Met Val Arg Gly Gln Val
 1               5                  10                  15

TTC GAC GTG GGG CCG CGC TAC ACT AAT CTC TCG TAC ATC GGA GAA GGC      96
Phe Asp Val Gly Pro Arg Tyr Thr Asn Leu Ser Tyr Ile Gly Glu Gly
            20                  25                  30

GCC TAC GGC ATG GTT TGT TCT GCT TAT GAT AAT CTC AAC AAA GTT CGA     144
Ala Tyr Gly Met Val Cys Ser Ala Tyr Asp Asn Leu Asn Lys Val Arg
        35                  40                  45

GTT GCT ATC AAG AAA ATC AGT CCT TTT GAG CAC CAG ACC TAC TGT CAG     192
Val Ala Ile Lys Lys Ile Ser Pro Phe Glu His Gln Thr Tyr Cys Gln
    50                  55                  60

AGA ACC CTG AGA GAG ATA AAA ATC CTA CTG CGC TTC AGA CAT GAG AAC     240
Arg Thr Leu Arg Glu Ile Lys Ile Leu Leu Arg Phe Arg His Glu Asn
65                  70                  75                  80
```

```
ATC ATC GGC ATC AAT GAC ATC ATC CGG GCA CCA ACC ATT GAG CAG ATG      288
Ile Ile Gly Ile Asn Asp Ile Ile Arg Ala Pro Thr Ile Glu Gln Met
                85                  90                  95

AAA GAT GTA TAT ATA GTA CAG GAC CTC ATG GAG ACA GAT CTT TAC AAG      336
Lys Asp Val Tyr Ile Val Gln Asp Leu Met Glu Thr Asp Leu Tyr Lys
            100                 105                 110

CTC TTG AAG ACA CAG CAC CTC AGC AAT GAT CAT ATC TGC TAT TTT CTT      384
Leu Leu Lys Thr Gln His Leu Ser Asn Asp His Ile Cys Tyr Phe Leu
        115                 120                 125

TAT CAG ATC CTG AGA GGA TTA AAG TAT ATA CAT TCA GCT AAT GTT CTG      432
Tyr Gln Ile Leu Arg Gly Leu Lys Tyr Ile His Ser Ala Asn Val Leu
    130                 135                 140

CAC CGT GAC CTC AAG CCT TCC AAC CTC CTG CTG AAC ACC ACT TGT GAT      480
His Arg Asp Leu Lys Pro Ser Asn Leu Leu Leu Asn Thr Thr Cys Asp
145                 150                 155                 160

CTC AAG ATC TGT GAC TTT GGC CTT GCC CGT GTT GCA GAT CCA GAC CAT      528
Leu Lys Ile Cys Asp Phe Gly Leu Ala Arg Val Ala Asp Pro Asp His
                165                 170                 175

GAT CAT ACA GGG TTC TTG ACA GAG TAT GTA GCC ACG CGT TGG TAC AGA      576
Asp His Thr Gly Phe Leu Thr Glu Tyr Val Ala Thr Arg Trp Tyr Arg
            180                 185                 190

GCT CCA GAA ATT ATG TTG AAT TCC AAG GGT TAT ACC AAG TCC ATT GAT      624
Ala Pro Glu Ile Met Leu Asn Ser Lys Gly Tyr Thr Lys Ser Ile Asp
        195                 200                 205

ATT TGG TCT GTG GGC TGC ATC CTG GCA GAG ATG CTA TCC AAC AGG CCT      672
Ile Trp Ser Val Gly Cys Ile Leu Ala Glu Met Leu Ser Asn Arg Pro
    210                 215                 220

ATC TTC CCA GGA AAG CAT TAC CTT GAC CAG CTG AAT CAC ATC CTG GGT      720
Ile Phe Pro Gly Lys His Tyr Leu Asp Gln Leu Asn His Ile Leu Gly
225                 230                 235                 240

ATT CTT GGA TCT CCA TCA CAG GAA GAT CTG AAT TGT ATA ATA AAT TTA      768
Ile Leu Gly Ser Pro Ser Gln Glu Asp Leu Asn Cys Ile Ile Asn Leu
                245                 250                 255

AAA GCT AGA AAC TAT TTG CTT TCT CTC CCG CAC AAA AAT AAG GTG CCG      816
Lys Ala Arg Asn Tyr Leu Leu Ser Leu Pro His Lys Asn Lys Val Pro
            260                 265                 270

TGG AAC AGG TTG TTC CCA AAC GCT GAC TCC AAA GCT CTG GAT TTA CTG      864
Trp Asn Arg Leu Phe Pro Asn Ala Asp Ser Lys Ala Leu Asp Leu Leu
        275                 280                 285

GAT AAA ATG TTG ACA TTT AAC CCT CAC AAG AGG ATT GAA GTT GAA CAG      912
Asp Lys Met Leu Thr Phe Asn Pro His Lys Arg Ile Glu Val Glu Gln
    290                 295                 300
```


BNSDOCID: <WO___9845704A2_I_>

```
GCT CTG GCC CAC CCG TAC CTG GAG CAG TAT TAT GAC CCA AGT GAT GAG      960
Ala Leu Ala His Pro Tyr Leu Glu Gln Tyr Tyr Asp Pro Ser Asp Glu
305                 310                 315                 320

CCC ATT GCT GAA GCA CCA TTC AAG TTT GAC ATG GAG CTG GAC GAC TTA     1008
Pro Ile Ala Glu Ala Pro Phe Lys Phe Asp Met Glu Leu Asp Asp Leu
                325                 330                 335

CCT AAG GAG AAG CTC AAA GAA CTC ATT TTT GAA GAG ACT GCT CGA TTC     1056
Pro Lys Glu Lys Leu Lys Glu Leu Ile Phe Glu Glu Thr Ala Arg Phe
            340                 345                 350

CAG CCA GGA TAC AGA TCT ATG GAT CCA CCG GTC GCC ACC ATG GTG AGC     1104
Gln Pro Gly Tyr Arg Ser Met Asp Pro Pro Val Ala Thr Met Val Ser
        355                 360                 365

AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG GTC GAG CTG     1152
Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu
    370                 375                 380

GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC GAG GGC GAG     1200
Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu
385                 390                 395                 400

GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC TGC ACC ACC     1248
Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr
                405                 410                 415

GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC CTG ACC TAC     1296
Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Thr Tyr
            420                 425                 430

GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG CAG CAC GAC     1344
Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln His Asp
        435                 440                 445

TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG CGC ACC ATC     1392
Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile
    450                 455                 460

TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG GTG AAG TTC     1440
Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe
465                 470                 475                 480

GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC ATC GAC TTC     1488
Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe
                485                 490                 495

AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC AAC TAC AAC     1536
Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn
            500                 505                 510

AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC GGC ATC AAG     1584
Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys
        515                 520                 525
```

```
GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC GTG CAG CTC    1632
Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu
    530                 535                 540

GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC CCC GTG CTG    1680
Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu
545                 550                 555                 560

CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG AGC AAA GAC    1728
Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp
                565                 570                 575

CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC GTG ACC GCC    1776
Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala
            580                 585                 590

GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AA GTAA                1815
Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
        595                 600
```

(2) INFORMATION FOR SEQ ID NO:59:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 604 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:

```
Met Ala Ala Ala Ala Ala Ala Gly Pro Glu Met Val Arg Gly Gln Val
 1               5                  10                  15
Phe Asp Val Gly Pro Arg Tyr Thr Asn Leu Ser Tyr Ile Gly Glu Gly
            20                  25                  30
Ala Tyr Gly Met Val Cys Ser Ala Tyr Asp Asn Leu Asn Lys Val Arg
        35                  40                  45
Val Ala Ile Lys Lys Ile Ser Pro Phe Glu His Gln Thr Tyr Cys Gln
    50                  55                  60
Arg Thr Leu Arg Glu Ile Lys Ile Leu Leu Arg Phe Arg His Glu Asn
65                  70                  75                  80
Ile Ile Gly Ile Asn Asp Ile Ile Arg Ala Pro Thr Ile Glu Gln Met
                85                  90                  95
Lys Asp Val Tyr Ile Val Gln Asp Leu Met Glu Thr Asp Leu Tyr Lys
            100                 105                 110
Leu Leu Lys Thr Gln His Leu Ser Asn Asp His Ile Cys Tyr Phe Leu
        115                 120                 125
Tyr Gln Ile Leu Arg Gly Leu Lys Tyr Ile His Ser Ala Asn Val Leu
    130                 135                 140
His Arg Asp Leu Lys Pro Ser Asn Leu Leu Leu Asn Thr Thr Cys Asp
145                 150                 155                 160
Leu Lys Ile Cys Asp Phe Gly Leu Ala Arg Val Ala Asp Pro Asp His
```


BNSDOCID: <WO___9845704A2_I_>

```
                                                                  165                 170                 175
Asp His Thr Gly Phe Leu Thr Glu Tyr Val Ala Thr Arg Trp Tyr Arg
            180                 185                 190
Ala Pro Glu Ile Met Leu Asn Ser Lys Gly Tyr Thr Lys Ser Ile Asp
        195                 200                 205
Ile Trp Ser Val Gly Cys Ile Leu Ala Glu Met Leu Ser Asn Arg Pro
    210                 215                 220
Ile Phe Pro Gly Lys His Tyr Leu Asp Gln Leu Asn His Ile Leu Gly
225                 230                 235                 240
Ile Leu Gly Ser Pro Ser Gln Glu Asp Leu Asn Cys Ile Ile Asn Leu
                245                 250                 255
Lys Ala Arg Asn Tyr Leu Leu Ser Leu Pro His Lys Asn Lys Val Pro
            260                 265                 270
Trp Asn Arg Leu Phe Pro Asn Ala Asp Ser Lys Ala Leu Asp Leu Leu
        275                 280                 285
Asp Lys Met Leu Thr Phe Asn Pro His Lys Arg Ile Glu Val Glu Gln
    290                 295                 300
Ala Leu Ala His Pro Tyr Leu Glu Gln Tyr Tyr Asp Pro Ser Asp Glu
305                 310                 315                 320
Pro Ile Ala Glu Ala Pro Phe Lys Phe Asp Met Glu Leu Asp Asp Leu
                325                 330                 335
Pro Lys Glu Lys Leu Lys Glu Leu Ile Phe Glu Glu Thr Ala Arg Phe
            340                 345                 350
Gln Pro Gly Tyr Arg Ser Met Asp Pro Pro Val Ala Thr Met Val Ser
        355                 360                 365
Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu
    370                 375                 380
Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu
385                 390                 395                 400
Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr
                405                 410                 415
Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Thr Tyr
            420                 425                 430
Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln His Asp
        435                 440                 445
Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile
    450                 455                 460
Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe
465                 470                 475                 480
Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe
                485                 490                 495
Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn
            500                 505                 510
Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys
        515                 520                 525
Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu
    530                 535                 540
Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu
545                 550                 555                 560
Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp
                565                 570                 575
Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala
            580                 585                 590
Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
        595                 600
```

(2) INFORMATION FOR SEQ ID NO:60:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2511 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...2508
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:

```
ATG GAG CTG GAA AAC ATC GTG GCC AAC ACG GTC TTG CTG AAA GCC AGG      48
Met Glu Leu Glu Asn Ile Val Ala Asn Thr Val Leu Leu Lys Ala Arg
 1               5                  10                  15

GAA GGG GGC GGA GGA AAG CGC AAA GGG AAA AGC AAG AAG TGG AAA GAA      96
Glu Gly Gly Gly Gly Lys Arg Lys Gly Lys Ser Lys Lys Trp Lys Glu
            20                  25                  30

ATC CTG AAG TTC CCT CAC ATT AGC CAG TGT GAA GAC CTC CGA AGG ACC     144
Ile Leu Lys Phe Pro His Ile Ser Gln Cys Glu Asp Leu Arg Arg Thr
        35                  40                  45

ATA GAC AGA GAT TAC TGC AGT TTA TGT GAC AAG CAG CCA ATC GGG AGG     192
Ile Asp Arg Asp Tyr Cys Ser Leu Cys Asp Lys Gln Pro Ile Gly Arg
    50                  55                  60

CTG CTT TTC CGG CAG TTT TGT GAA ACC AGG CCT GGG CTG GAG TGT TAC     240
Leu Leu Phe Arg Gln Phe Cys Glu Thr Arg Pro Gly Leu Glu Cys Tyr
65                  70                  75                  80

ATT CAG TTC CTG GAC TCC GTG GCA GAA TAT GAA GTT ACT CCA GAT GAA     288
Ile Gln Phe Leu Asp Ser Val Ala Glu Tyr Glu Val Thr Pro Asp Glu
                85                  90                  95

AAA CTG GGA GAG AAA GGG AAG GAA ATT ATG ACC AAG TAC CTC ACC CCA     336
Lys Leu Gly Glu Lys Gly Lys Glu Ile Met Thr Lys Tyr Leu Thr Pro
            100                 105                 110

AAG TCC CCT GTT TTC ATA GCC CAA GTT GGC CAA GAC CTG GTC TCC CAG     384
Lys Ser Pro Val Phe Ile Ala Gln Val Gly Gln Asp Leu Val Ser Gln
        115                 120                 125

ACG GAG GAG AAG CTC CTA CAG AAG CCG TGC AAA GAA CTC TTT TCT GCC     432
Thr Glu Glu Lys Leu Leu Gln Lys Pro Cys Lys Glu Leu Phe Ser Ala
    130                 135                 140

TGT GCA CAG TCT GTC CAC GAG TAC CTG AGG GGA GAA CCA TTC CAC GAA     480
Cys Ala Gln Ser Val His Glu Tyr Leu Arg Gly Glu Pro Phe His Glu
145                 150                 155                 160
```

```
TAT CTG GAC AGC ATG TTT TTT GAC CGC TTT CTC CAG TGG AAG TGG TTG      528
Tyr Leu Asp Ser Met Phe Phe Asp Arg Phe Leu Gln Trp Lys Trp Leu
                165                 170                 175

GAA AGG CAA CCG GTG ACC AAA AAC ACT TTC AGG CAG TAT CGA GTG CTA      576
Glu Arg Gln Pro Val Thr Lys Asn Thr Phe Arg Gln Tyr Arg Val Leu
            180                 185                 190

GGA AAA GGG GGC TTC GGG GAG GTC TGT GCC TGC CAG GTT CGG GCC ACG      624
Gly Lys Gly Gly Phe Gly Glu Val Cys Ala Cys Gln Val Arg Ala Thr
        195                 200                 205

GGT AAA ATG TAT GCC TGC AAG CGC TTG GAG AAG AAG AGG ATC AAA AAG      672
Gly Lys Met Tyr Ala Cys Lys Arg Leu Glu Lys Lys Arg Ile Lys Lys
    210                 215                 220

AGG AAA GGG GAG TCC ATG GCC CTC AAT GAG AAG CAG ATC CTC GAG AAG      720
Arg Lys Gly Glu Ser Met Ala Leu Asn Glu Lys Gln Ile Leu Glu Lys
225                 230                 235                 240

GTC AAC AGT CAG TTT GTG GTC AAC CTG GCC TAT GCC TAC GAG ACC AAG      768
Val Asn Ser Gln Phe Val Val Asn Leu Ala Tyr Ala Tyr Glu Thr Lys
                245                 250                 255

GAT GCA CTG TGC TTG GTC CTG ACC ATC ATG AAT GGG GGT GAC CTG AAG      816
Asp Ala Leu Cys Leu Val Leu Thr Ile Met Asn Gly Gly Asp Leu Lys
            260                 265                 270

TTC CAC ATC TAC AAC ATG GGC AAC CCT GGC TTC GAG GAG GAG CGG GCC      864
Phe His Ile Tyr Asn Met Gly Asn Pro Gly Phe Glu Glu Glu Arg Ala
        275                 280                 285

TTG TTT TAT GCG GCA GAG ATC CTC TGC GGC TTA GAA GAC CTC CAC CGT      912
Leu Phe Tyr Ala Ala Glu Ile Leu Cys Gly Leu Glu Asp Leu His Arg
    290                 295                 300

GAG AAC ACC GTC TAC CGA GAT CTG AAA CCT GAA AAC ATC CTG TTA GAT      960
Glu Asn Thr Val Tyr Arg Asp Leu Lys Pro Glu Asn Ile Leu Leu Asp
305                 310                 315                 320

GAT TAT GGC CAC ATT AGG ATC TCA GAC CTG GGC TTG GCT GTG AAG ATC     1008
Asp Tyr Gly His Ile Arg Ile Ser Asp Leu Gly Leu Ala Val Lys Ile
                325                 330                 335

CCC GAG GGA GAC CTG ATC CGC GGC CGG GTG GGC ACT GTT GGC TAC ATG     1056
Pro Glu Gly Asp Leu Ile Arg Gly Arg Val Gly Thr Val Gly Tyr Met
            340                 345                 350

GCC CCC GAA GTC CTG AAC AAC CAG AGG TAC GGC CTG AGC CCC GAC TAC     1104
Ala Pro Glu Val Leu Asn Asn Gln Arg Tyr Gly Leu Ser Pro Asp Tyr
        355                 360                 365

TGG GGC CTT GGC TGC CTC ATC TAT GAG ATG ATC GAG GGC CAG TCG CCG     1152
Trp Gly Leu Gly Cys Leu Ile Tyr Glu Met Ile Glu Gly Gln Ser Pro
    370                 375                 380
```

```
TTC CGC GGC CGT AAG GAG AAG GTG AAG CGG GAG GAG GTG GAC CGC CGG    1200
Phe Arg Gly Arg Lys Glu Lys Val Lys Arg Glu Glu Val Asp Arg Arg
385                 390                 395                 400

GTC CTG GAG ACG GAG GAG GTG TAC TCC CAC AAG TTC TCC GAG GAG GCC    1248
Val Leu Glu Thr Glu Glu Val Tyr Ser His Lys Phe Ser Glu Glu Ala
                405                 410                 415

AAG TCC ATC TGC AAG ATG CTG CTC ACG AAA GAT GCG AAG CAG AGG CTG    1296
Lys Ser Ile Cys Lys Met Leu Leu Thr Lys Asp Ala Lys Gln Arg Leu
            420                 425                 430

GGC TGC CAG GAG GAG GGG GCT GCA GAG GTC AAG AGA CAC CCC TTC TTC    1344
Gly Cys Gln Glu Glu Gly Ala Ala Glu Val Lys Arg His Pro Phe Phe
        435                 440                 445

AGG AAC ATG AAC TTC AAG CGC TTA GAA GCC GGG ATG TTG GAC CCT CCC    1392
Arg Asn Met Asn Phe Lys Arg Leu Glu Ala Gly Met Leu Asp Pro Pro
    450                 455                 460

TTC GTT CCA GAC CCC CGC GCT GTG TAC TGT AAG GAC GTG CTG GAC ATC    1440
Phe Val Pro Asp Pro Arg Ala Val Tyr Cys Lys Asp Val Leu Asp Ile
465                 470                 475                 480

GAG CAG TTC TCC ACT GTG AAG GGC GTC AAT CTG GAC CAC ACA GAC GAC    1488
Glu Gln Phe Ser Thr Val Lys Gly Val Asn Leu Asp His Thr Asp Asp
                485                 490                 495

GAC TTC TAC TCC AAG TTC TCC ACG GGC TCT GTG TCC ATC CCA TGG CAA    1536
Asp Phe Tyr Ser Lys Phe Ser Thr Gly Ser Val Ser Ile Pro Trp Gln
            500                 505                 510

AAC GAG ATG ATA GAA ACA GAA TGC TTT AAG GAG CTG AAC GTG TTT GGA    1584
Asn Glu Met Ile Glu Thr Glu Cys Phe Lys Glu Leu Asn Val Phe Gly
        515                 520                 525

CCT AAT GGT ACC CTC CCG CCA GAT CTG AAC AGA AAC CAC CCT CCG GAA    1632
Pro Asn Gly Thr Leu Pro Pro Asp Leu Asn Arg Asn His Pro Pro Glu
    530                 535                 540

CCG CCC AAG AAA GGG CTG CTC CAG AGA CTC TTC AAG CGG CAG CAT CAG    1680
Pro Pro Lys Lys Gly Leu Leu Gln Arg Leu Phe Lys Arg Gln His Gln
545                 550                 555                 560

AAC AAT TCC AAG AGT TCG CCC AGC TCC AAG ACC AGT TTT AAC CAC CAC    1728
Asn Asn Ser Lys Ser Ser Pro Ser Ser Lys Thr Ser Phe Asn His His
                565                 570                 575

ATA AAC TCA AAC CAT GTC AGC TCG AAC TCC ACC GGA AGC AGC AGG GAT    1776
Ile Asn Ser Asn His Val Ser Ser Asn Ser Thr Gly Ser Ser Arg Asp
            580                 585                 590

CCA CCG GTC GCC ACC ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG    1824
Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly
        595                 600                 605
```

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GTG GTG CCC ATC CTG GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG      1872
Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys
    610                 615                 620

TTC AGC GTG TCC GGC GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG      1920
Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu
625                 630                 635                 640

ACC CTG AAG TTC ATC TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC      1968
Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro
                645                 650                 655

ACC CTC GTG ACC ACC CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC      2016
Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr
            660                 665                 670

CCC GAC CAC ATG AAG CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA      2064
Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu
        675                 680                 685

GGC TAC GTC CAG GAG CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC      2112
Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr
    690                 695                 700

AAG ACC CGC GCC GAG GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC      2160
Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg
705                 710                 715                 720

ATC GAG CTG AAG GGC ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG      2208
Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly
                725                 730                 735

CAC AAG CTG GAG TAC AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC      2256
His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala
            740                 745                 750

GAC AAG CAG AAG AAC GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC      2304
Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn
        755                 760                 765

ATC GAG GAC GGC AGC GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC      2352
Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr
    770                 775                 780

CCC ATC GGC GAC GGC CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC      2400
Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser
785                 790                 795                 800

ACC CAG TCC GCC CTG AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG      2448
Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met
                805                 810                 815

GTC CTG CTG GAG TTC GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC      2496
Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp
            820                 825                 830
```

GAG CTG TAC AAG TAA 2511
Glu Leu Tyr Lys
835

(2) INFORMATION FOR SEQ ID NO:61:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 836 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:61:

Met Glu Leu Glu Asn Ile Val Ala Asn Thr Val Leu Leu Lys Ala Arg
1 5 10 15
Glu Gly Gly Gly Gly Lys Arg Lys Gly Lys Ser Lys Lys Trp Lys Glu
20 25 30
Ile Leu Lys Phe Pro His Ile Ser Gln Cys Glu Asp Leu Arg Arg Thr
35 40 45
Ile Asp Arg Asp Tyr Cys Ser Leu Cys Asp Lys Gln Pro Ile Gly Arg
50 55 60
Leu Leu Phe Arg Gln Phe Cys Glu Thr Arg Pro Gly Leu Glu Cys Tyr
65 70 75 80
Ile Gln Phe Leu Asp Ser Val Ala Glu Tyr Glu Val Thr Pro Asp Glu
85 90 95
Lys Leu Gly Glu Lys Gly Lys Glu Ile Met Thr Lys Tyr Leu Thr Pro
100 105 110
Lys Ser Pro Val Phe Ile Ala Gln Val Gly Gln Asp Leu Val Ser Gln
115 120 125
Thr Glu Glu Lys Leu Leu Gln Lys Pro Cys Lys Glu Leu Phe Ser Ala
130 135 140
Cys Ala Gln Ser Val His Glu Tyr Leu Arg Gly Glu Pro Phe His Glu
145 150 155 160
Tyr Leu Asp Ser Met Phe Phe Asp Arg Phe Leu Gln Trp Lys Trp Leu
165 170 175
Glu Arg Gln Pro Val Thr Lys Asn Thr Phe Arg Gln Tyr Arg Val Leu
180 185 190
Gly Lys Gly Gly Phe Gly Glu Val Cys Ala Cys Gln Val Arg Ala Thr
195 200 205
Gly Lys Met Tyr Ala Cys Lys Arg Leu Glu Lys Lys Arg Ile Lys Lys
210 215 220
Arg Lys Gly Glu Ser Met Ala Leu Asn Glu Lys Gln Ile Leu Glu Lys
225 230 235 240
Val Asn Ser Gln Phe Val Val Asn Leu Ala Tyr Ala Tyr Glu Thr Lys
245 250 255
Asp Ala Leu Cys Leu Val Leu Thr Ile Met Asn Gly Gly Asp Leu Lys
260 265 270
Phe His Ile Tyr Asn Met Gly Asn Pro Gly Phe Glu Glu Glu Arg Ala
275 280 285
Leu Phe Tyr Ala Ala Glu Ile Leu Cys Gly Leu Glu Asp Leu His Arg

290 295 300
Glu Asn Thr Val Tyr Arg Asp Leu Lys Pro Glu Asn Ile Leu Leu Asp
305 310 315 320
Asp Tyr Gly His Ile Arg Ile Ser Asp Leu Gly Leu Ala Val Lys Ile
325 330 335
Pro Glu Gly Asp Leu Ile Arg Gly Arg Val Gly Thr Val Gly Tyr Met
340 345 350
Ala Pro Glu Val Leu Asn Asn Gln Arg Tyr Gly Leu Ser Pro Asp Tyr
355 360 365
Trp Gly Leu Gly Cys Leu Ile Tyr Glu Met Ile Glu Gly Gln Ser Pro
370 375 380
Phe Arg Gly Arg Lys Glu Lys Val Lys Arg Glu Glu Val Asp Arg Arg
385 390 395 400
Val Leu Glu Thr Glu Glu Val Tyr Ser His Lys Phe Ser Glu Glu Ala
405 410 415
Lys Ser Ile Cys Lys Met Leu Leu Thr Lys Asp Ala Lys Gln Arg Leu
420 425 430
Gly Cys Gln Glu Glu Gly Ala Ala Glu Val Lys Arg His Pro Phe Phe
435 440 445
Arg Asn Met Asn Phe Lys Arg Leu Glu Ala Gly Met Leu Asp Pro Pro
450 455 460
Phe Val Pro Asp Pro Arg Ala Val Tyr Cys Lys Asp Val Leu Asp Ile
465 470 475 480
Glu Gln Phe Ser Thr Val Lys Gly Val Asn Leu Asp His Thr Asp Asp
485 490 495
Asp Phe Tyr Ser Lys Phe Ser Thr Gly Ser Val Ser Ile Pro Trp Gln
500 505 510
Asn Glu Met Ile Glu Thr Glu Cys Phe Lys Glu Leu Asn Val Phe Gly
515 520 525
Pro Asn Gly Thr Leu Pro Pro Asp Leu Asn Arg Asn His Pro Pro Glu
530 535 540
Pro Pro Lys Lys Gly Leu Leu Gln Arg Leu Phe Lys Arg Gln His Gln
545 550 555 560
Asn Asn Ser Lys Ser Ser Pro Ser Ser Lys Thr Ser Phe Asn His His
565 570 575
Ile Asn Ser Asn His Val Ser Ser Asn Ser Thr Gly Ser Ser Arg Asp
580 585 590
Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly
595 600 605
Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys
610 615 620
Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu
625 630 635 640
Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro
645 650 655
Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr
660 665 670
Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu
675 680 685
Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr
690 695 700
Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg
705 710 715 720
Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly
725 730 735
His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala

740 745 750
Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn
755 760 765
Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr
770 775 780
Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser
785 790 795 800
Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met
805 810 815
Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp
820 825 830
Glu Leu Tyr Lys
835

(2) INFORMATION FOR SEQ ID NO:62:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1893 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...1890
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:62:

```
ATG AGC AGA AGC AAG CGT GAC AAC AAT TTT TAT AGT GTA GAG ATT GGA      48
Met Ser Arg Ser Lys Arg Asp Asn Asn Phe Tyr Ser Val Glu Ile Gly
 1               5                  10                  15

GAT TCT ACA TTC ACA GTC CTG AAA CGA TAT CAG AAT TTA AAA CCT ATA      96
Asp Ser Thr Phe Thr Val Leu Lys Arg Tyr Gln Asn Leu Lys Pro Ile
            20                  25                  30

GGC TCA GGA GCT CAA GGA ATA GTA TGC GCA GCT TAT GAT GCC ATT CTT     144
Gly Ser Gly Ala Gln Gly Ile Val Cys Ala Ala Tyr Asp Ala Ile Leu
        35                  40                  45

GAA AGA AAT GTT GCA ATC AAG AAG CTA AGC CGA CCA TTT CAG AAT CAG     192
Glu Arg Asn Val Ala Ile Lys Lys Leu Ser Arg Pro Phe Gln Asn Gln
    50                  55                  60

ACT CAT GCC AAG CGG GCC TAC AGA GAG CTA GTT CTT ATG AAA TGT GTT     240
Thr His Ala Lys Arg Ala Tyr Arg Glu Leu Val Leu Met Lys Cys Val
65                  70                  75                  80

AAT CAC AAA AAT ATA ATT GGC CTT TTG AAT GTT TTC ACA CCA CAG AAA     288
Asn His Lys Asn Ile Ile Gly Leu Leu Asn Val Phe Thr Pro Gln Lys
                85                  90                  95

TCC CTA GAA GAA TTT CAA GAT GTT TAC ATA GTC ATG GAG CTC ATG GAT     336
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```
Ser Leu Glu Glu Phe Gln Asp Val Tyr Ile Val Met Glu Leu Met Asp
100                 105                 110

GCA AAT CTT TGC CAA GTG ATT CAG ATG GAG CTA GAT CAT GAA AGA ATG      384
Ala Asn Leu Cys Gln Val Ile Gln Met Glu Leu Asp His Glu Arg Met
115                 120                 125

TCC TAC CTT CTC TAT CAG ATG CTG TGT GGA ATC AAG CAC CTT CAT TCT      432
Ser Tyr Leu Leu Tyr Gln Met Leu Cys Gly Ile Lys His Leu His Ser
130                 135                 140

GCT GGA ATT ATT CAT CGG GAC TTA AAG CCC AGT AAT ATA GTA GTA AAA      480
Ala Gly Ile Ile His Arg Asp Leu Lys Pro Ser Asn Ile Val Val Lys
145                 150                 155                 160

TCT GAT TGC ACT TTG AAG ATT CTT GAC TTC GGT CTG GCC AGG ACT GCA      528
Ser Asp Cys Thr Leu Lys Ile Leu Asp Phe Gly Leu Ala Arg Thr Ala
165                 170                 175

GGA ACG AGT TTT ATG ATG ACG CCT TAT GTA GTG ACT CGC TAC TAC AGA      576
Gly Thr Ser Phe Met Met Thr Pro Tyr Val Val Thr Arg Tyr Tyr Arg
180                 185                 190

GCA CCC GAG GTC ATC CTT GGC ATG GGC TAC AAG GAA AAC GTG GAT TTA      624
Ala Pro Glu Val Ile Leu Gly Met Gly Tyr Lys Glu Asn Val Asp Leu
195                 200                 205

TGG TCT GTG GGG TGC ATT ATG GGA GAA ATG GTT TGC CAC AAA ATC CTC      672
Trp Ser Val Gly Cys Ile Met Gly Glu Met Val Cys His Lys Ile Leu
210                 215                 220

TTT CCA GGA AGG GAC TAT ATT GAT CAG TGG AAT AAA GTT ATT GAA CAG      720
Phe Pro Gly Arg Asp Tyr Ile Asp Gln Trp Asn Lys Val Ile Glu Gln
225                 230                 235                 240

CTT GGA ACA CCA TGT CCT GAA TTC ATG AAG AAA CTG CAA CCA ACA GTA      768
Leu Gly Thr Pro Cys Pro Glu Phe Met Lys Lys Leu Gln Pro Thr Val
245                 250                 255

AGG ACT TAC GTT GAA AAC AGA CCT AAA TAT GCT GGA TAT AGC TTT GAG      816
Arg Thr Tyr Val Glu Asn Arg Pro Lys Tyr Ala Gly Tyr Ser Phe Glu
260                 265                 270

AAA CTC TTC CCT GAT GTC CTT TTC CCA GCT GAC TCA GAA CAC AAC AAA      864
Lys Leu Phe Pro Asp Val Leu Phe Pro Ala Asp Ser Glu His Asn Lys
275                 280                 285

CTT AAA GCC AGT CAG GCA AGG GAT TTG TTA TCC AAA ATG CTG GTA ATA      912
Leu Lys Ala Ser Gln Ala Arg Asp Leu Leu Ser Lys Met Leu Val Ile
290                 295                 300

GAT GCA TCT AAA AGG ATC TCT GTA GAT GAA GCT CTC CAA CAC CCG TAC      960
Asp Ala Ser Lys Arg Ile Ser Val Asp Glu Ala Leu Gln His Pro Tyr
305                 310                 315                 320

ATC AAT GTC TGG TAT GAT CCT TCT GAA GCA GAA GCT CCA CCA CCA AAG     1008
```

```
Ile Asn Val Trp Tyr Asp Pro Ser Glu Ala Glu Ala Pro Pro Pro Lys
                  325                 330                 335

ATC CCT GAC AAG CAG TTA GAT GAA AGG GAA CAC ACA ATA GAA GAG TGG    1056
Ile Pro Asp Lys Gln Leu Asp Glu Arg Glu His Thr Ile Glu Glu Trp
            340                 345                 350

AAA GAA TTG ATA TAT AAG GAA GTT ATG GAC TTG GAG GAG AGA ACC AAG    1104
Lys Glu Leu Ile Tyr Lys Glu Val Met Asp Leu Glu Glu Arg Thr Lys
        355                 360                 365

AAT GGA GTT ATA CGG GGG CAG CCC TCT CCT TTA GCA CAG GTG CAG CAG    1152
Asn Gly Val Ile Arg Gly Gln Pro Ser Pro Leu Ala Gln Val Gln Gln
    370                 375                 380

TGG GAT CCA CCG GTC GCC ACC ATG GTG AGC AAG GGC GAG GAG CTG TTC    1200
Trp Asp Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe
385                 390                 395                 400

ACC GGG GTG GTG CCC ATC CTG GTC GAG CTG GAC GGC GAC GTA AAC GGC    1248
Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly
                  405                 410                 415

CAC AAG TTC AGC GTG TCC GGC GAG GGC GAG GGC GAT GCC ACC TAC GGC    1296
His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly
            420                 425                 430

AAG CTG ACC CTG AAG TTC ATC TGC ACC ACC GGC AAG CTG CCC GTG CCC    1344
Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro
        435                 440                 445

TGG CCC ACC CTC GTG ACC ACC CTG ACC TAC GGC GTG CAG TGC TTC AGC    1392
Trp Pro Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser
    450                 455                 460

CGC TAC CCC GAC CAC ATG AAG CAG CAC GAC TTC TTC AAG TCC GCC ATG    1440
Arg Tyr Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met
465                 470                 475                 480

CCC GAA GGC TAC GTC CAG GAG CGC ACC ATC TTC TTC AAG GAC GAC GGC    1488
Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly
                  485                 490                 495

AAC TAC AAG ACC CGC GCC GAG GTG AAG TTC GAG GGC GAC ACC CTG GTG    1536
Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val
            500                 505                 510

AAC CGC ATC GAG CTG AAG GGC ATC GAC TTC AAG GAG GAC GGC AAC ATC    1584
Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile
        515                 520                 525

CTG GGG CAC AAG CTG GAG TAC AAC TAC AAC AGC CAC AAC GTC TAT ATC    1632
Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile
    530                 535                 540

ATG GCC GAC AAG CAG AAG AAC GGC ATC AAG GTG AAC TTC AAG ATC CGC    1680
```

```
Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg
545                 550                 555                 560

CAC AAC ATC GAG GAC GGC AGC GTG CAG CTC GCC GAC CAC TAC CAG CAG    1728
His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln
                565                 570                 575

AAC ACC CCC ATC GGC GAC GGC CCC GTG CTG CTG CCC GAC AAC CAC TAC    1776
Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr
            580                 585                 590

CTG AGC ACC CAG TCC GCC CTG AGC AAA GAC CCC AAC GAG AAG CGC GAT    1824
Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp
        595                 600                 605

CAC ATG GTC CTG CTG GAG TTC GTG ACC GCC GCC GGG ATC ACT CTC GGC    1872
His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly
    610                 615                 620

ATG GAC GAG CTG TAC AAG TAA                                        1893
Met Asp Glu Leu Tyr Lys
625                 630
```

(2) INFORMATION FOR SEQ ID NO:63:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 630 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:

```
Met Ser Arg Ser Lys Arg Asp Asn Asn Phe Tyr Ser Val Glu Ile Gly
 1               5                  10                  15
Asp Ser Thr Phe Thr Val Leu Lys Arg Tyr Gln Asn Leu Lys Pro Ile
            20                  25                  30
Gly Ser Gly Ala Gln Gly Ile Val Cys Ala Ala Tyr Asp Ala Ile Leu
        35                  40                  45
Glu Arg Asn Val Ala Ile Lys Lys Leu Ser Arg Pro Phe Gln Asn Gln
    50                  55                  60
Thr His Ala Lys Arg Ala Tyr Arg Glu Leu Val Leu Met Lys Cys Val
65                  70                  75                  80
Asn His Lys Asn Ile Ile Gly Leu Leu Asn Val Phe Thr Pro Gln Lys
                85                  90                  95
Ser Leu Glu Glu Phe Gln Asp Val Tyr Ile Val Met Glu Leu Met Asp
            100                 105                 110
Ala Asn Leu Cys Gln Val Ile Gln Met Glu Leu Asp His Glu Arg Met
        115                 120                 125
Ser Tyr Leu Leu Tyr Gln Met Leu Cys Gly Ile Lys His Leu His Ser
    130                 135                 140
Ala Gly Ile Ile His Arg Asp Leu Lys Pro Ser Asn Ile Val Val Lys
```

```
145                 150                 155                 160
Ser Asp Cys Thr Leu Lys Ile Leu Asp Phe Gly Leu Ala Arg Thr Ala
                165                 170                 175
Gly Thr Ser Phe Met Met Thr Pro Tyr Val Val Thr Arg Tyr Tyr Arg
            180                 185                 190
Ala Pro Glu Val Ile Leu Gly Met Gly Tyr Lys Glu Asn Val Asp Leu
        195                 200                 205
Trp Ser Val Gly Cys Ile Met Gly Glu Met Val Cys His Lys Ile Leu
    210                 215                 220
Phe Pro Gly Arg Asp Tyr Ile Asp Gln Trp Asn Lys Val Ile Glu Gln
225                 230                 235                 240
Leu Gly Thr Pro Cys Pro Glu Phe Met Lys Lys Leu Gln Pro Thr Val
                245                 250                 255
Arg Thr Tyr Val Glu Asn Arg Pro Lys Tyr Ala Gly Tyr Ser Phe Glu
            260                 265                 270
Lys Leu Phe Pro Asp Val Leu Phe Pro Ala Asp Ser Glu His Asn Lys
        275                 280                 285
Leu Lys Ala Ser Gln Ala Arg Asp Leu Leu Ser Lys Met Leu Val Ile
    290                 295                 300
Asp Ala Ser Lys Arg Ile Ser Val Asp Glu Ala Leu Gln His Pro Tyr
305                 310                 315                 320
Ile Asn Val Trp Tyr Asp Pro Ser Glu Ala Glu Ala Pro Pro Pro Lys
                325                 330                 335
Ile Pro Asp Lys Gln Leu Asp Glu Arg Glu His Thr Ile Glu Glu Trp
            340                 345                 350
Lys Glu Leu Ile Tyr Lys Glu Val Met Asp Leu Glu Glu Arg Thr Lys
        355                 360                 365
Asn Gly Val Ile Arg Gly Gln Pro Ser Pro Leu Ala Gln Val Gln Gln
    370                 375                 380
Trp Asp Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe
385                 390                 395                 400
Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly
                405                 410                 415
His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly
            420                 425                 430
Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro
        435                 440                 445
Trp Pro Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser
    450                 455                 460
Arg Tyr Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met
465                 470                 475                 480
Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly
                485                 490                 495
Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val
            500                 505                 510
Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile
        515                 520                 525
Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile
    530                 535                 540
Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg
545                 550                 555                 560
His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln
                565                 570                 575
Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr
            580                 585                 590
Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp
```

595 600 605
His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly
610 615 620
Met Asp Glu Leu Tyr Lys
625 630

(2) INFORMATION FOR SEQ ID NO:64:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1821 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...1818
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:64:

ATG TCT CAG GAG AGG CCC ACG TTC TAC CGG CAG GAG CTG AAC AAG ACA 48
Met Ser Gln Glu Arg Pro Thr Phe Tyr Arg Gln Glu Leu Asn Lys Thr
1 5 10 15

ATC TGG GAG GTG CCC GAG CGT TAC CAG AAC CTG TCT CCA GTG GGC TCT 96
Ile Trp Glu Val Pro Glu Arg Tyr Gln Asn Leu Ser Pro Val Gly Ser
20 25 30

GGC GCC TAT GGC TCT GTG TGT GCT GCT TTT GAC ACA AAA ACG GGG TTA 144
Gly Ala Tyr Gly Ser Val Cys Ala Ala Phe Asp Thr Lys Thr Gly Leu
35 40 45

CGT GTG GCA GTG AAG AAG CTC TCC AGA CCA TTT CAG TCC ATC ATT CAT 192
Arg Val Ala Val Lys Lys Leu Ser Arg Pro Phe Gln Ser Ile Ile His
50 55 60

GCG AAA AGA ACC TAC AGA GAA CTG CGG TTA CTT AAA CAT ATG AAA CAT 240
Ala Lys Arg Thr Tyr Arg Glu Leu Arg Leu Leu Lys His Met Lys His
65 70 75 80

GAA AAT GTG ATT GGT CTG TTG GAC GTT TTT ACA CCT GCA AGG TCT CTG 288
Glu Asn Val Ile Gly Leu Leu Asp Val Phe Thr Pro Ala Arg Ser Leu
85 90 95

GAG GAA TTC AAT GAT GTG TAT CTG GTG ACC CAT CTC ATG GGG GCA GAT 336
Glu Glu Phe Asn Asp Val Tyr Leu Val Thr His Leu Met Gly Ala Asp
100 105 110

CTG AAC AAC ATT GTG AAA TGT CAG AAG CTT ACA GAT GAC CAT GTT CAG 384
Leu Asn Asn Ile Val Lys Cys Gln Lys Leu Thr Asp Asp His Val Gln
115 120 125

TTC CTT ATC TAC CAA ATT CTC CGA GGT CTA AAG TAT ATA CAT TCA GCT 432

```
Phe Leu Ile Tyr Gln Ile Leu Arg Gly Leu Lys Tyr Ile His Ser Ala
    130                 135                 140

GAC ATA ATT CAC AGG GAC CTA AAA CCT AGT AAT CTA GCT GTG AAT GAA     480
Asp Ile Ile His Arg Asp Leu Lys Pro Ser Asn Leu Ala Val Asn Glu
145                 150                 155                 160

GAC TGT GAG CTG AAG ATT CTG GAT TTT GGA CTG GCT CGG CAC ACA GAT     528
Asp Cys Glu Leu Lys Ile Leu Asp Phe Gly Leu Ala Arg His Thr Asp
                165                 170                 175

GAT GAA ATG ACA GGC TAC GTG GCC ACT AGG TGG TAC AGG GCT CCT GAG     576
Asp Glu Met Thr Gly Tyr Val Ala Thr Arg Trp Tyr Arg Ala Pro Glu
            180                 185                 190

ATC ATG CTG AAC TGG ATG CAT TAC AAC CAG ACA GTT GAT ATT TGG TCA     624
Ile Met Leu Asn Trp Met His Tyr Asn Gln Thr Val Asp Ile Trp Ser
        195                 200                 205

GTG GGA TGC ATA ATG GCC GAG CTG TTG ACT GGA AGA ACA TTG TTT CCT     672
Val Gly Cys Ile Met Ala Glu Leu Leu Thr Gly Arg Thr Leu Phe Pro
    210                 215                 220

GGT ACA GAC CAT ATT GAT CAG TTG AAG CTC ATT TTA AGA CTC GTT GGA     720
Gly Thr Asp His Ile Asp Gln Leu Lys Leu Ile Leu Arg Leu Val Gly
225                 230                 235                 240

ACC CCA GGG GCT GAG CTT TTG AAG AAA ATC TCC TCA GAG TCT GCA AGA     768
Thr Pro Gly Ala Glu Leu Leu Lys Lys Ile Ser Ser Glu Ser Ala Arg
                245                 250                 255

AAC TAT ATT CAG TCT TTG ACT CAG ATG CCG AAG ATG AAC TTT GCG AAT     816
Asn Tyr Ile Gln Ser Leu Thr Gln Met Pro Lys Met Asn Phe Ala Asn
            260                 265                 270

GTA TTT ATT GGT GCC AAT CCC CTG GCT GTC GAC TTG CTG GAG AAG ATG     864
Val Phe Ile Gly Ala Asn Pro Leu Ala Val Asp Leu Leu Glu Lys Met
        275                 280                 285

CTT GTA TTG GAC TCA GAT AAG AGA ATT ACA GCG GCC CAA GCC CTT GCA     912
Leu Val Leu Asp Ser Asp Lys Arg Ile Thr Ala Ala Gln Ala Leu Ala
    290                 295                 300

CAT GCC TAC TTT GCT CAG TAC CAC GAT CCT GAT GAT GAA CCA GTG GCC     960
His Ala Tyr Phe Ala Gln Tyr His Asp Pro Asp Asp Glu Pro Val Ala
305                 310                 315                 320

GAT CCT TAT GAT CAG TCC TTT GAA AGC AGG GAC CTC CTT ATA GAT GAG    1008
Asp Pro Tyr Asp Gln Ser Phe Glu Ser Arg Asp Leu Leu Ile Asp Glu
                325                 330                 335

TGG AAA AGC CTG ACC TAT GAT GAA GTC ATC AGC TTT GTG CCA CCA CCC    1056
Trp Lys Ser Leu Thr Tyr Asp Glu Val Ile Ser Phe Val Pro Pro Pro
            340                 345                 350

CTT GAC CAA GAA GAG ATG GAG TCC GAG GAT CCA CCG GTC GCC ACC ATG    1104
```

```
Leu Asp Gln Glu Glu Met Glu Ser Glu Asp Pro Pro Val Ala Thr Met
        355                 360                 365

GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG GTC    1152
Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val
    370                 375                 380

GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC GAG    1200
Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu
385                 390                 395                 400

GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC TGC    1248
Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys
                405                 410                 415

ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC CTG    1296
Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu
            420                 425                 430

ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG CAG    1344
Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln
        435                 440                 445

CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG CGC    1392
His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg
    450                 455                 460

ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG GTG    1440
Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val
465                 470                 475                 480

AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC ATC    1488
Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile
                485                 490                 495

GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC AAC    1536
Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn
            500                 505                 510

TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC GGC    1584
Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly
        515                 520                 525

ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC GTG    1632
Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val
    530                 535                 540

CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC CCC    1680
Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro
545                 550                 555                 560

GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG AGC    1728
Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser
                565                 570                 575

AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC GTG    1776
```

```
Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val
            580                 585                 590

ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TAA        1821
Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
        595                 600                 605
```

(2) INFORMATION FOR SEQ ID NO:65:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 606 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:

```
Met Ser Gln Glu Arg Pro Thr Phe Tyr Arg Gln Glu Leu Asn Lys Thr
 1               5                  10                  15
Ile Trp Glu Val Pro Glu Arg Tyr Gln Asn Leu Ser Pro Val Gly Ser
            20                  25                  30
Gly Ala Tyr Gly Ser Val Cys Ala Ala Phe Asp Thr Lys Thr Gly Leu
        35                  40                  45
Arg Val Ala Val Lys Lys Leu Ser Arg Pro Phe Gln Ser Ile Ile His
    50                  55                  60
Ala Lys Arg Thr Tyr Arg Glu Leu Arg Leu Leu Lys His Met Lys His
65                  70                  75                  80
Glu Asn Val Ile Gly Leu Leu Asp Val Phe Thr Pro Ala Arg Ser Leu
                85                  90                  95
Glu Glu Phe Asn Asp Val Tyr Leu Val Thr His Leu Met Gly Ala Asp
            100                 105                 110
Leu Asn Asn Ile Val Lys Cys Gln Lys Leu Thr Asp Asp His Val Gln
        115                 120                 125
Phe Leu Ile Tyr Gln Ile Leu Arg Gly Leu Lys Tyr Ile His Ser Ala
    130                 135                 140
Asp Ile Ile His Arg Asp Leu Lys Pro Ser Asn Leu Ala Val Asn Glu
145                 150                 155                 160
Asp Cys Glu Leu Lys Ile Leu Asp Phe Gly Leu Ala Arg His Thr Asp
                165                 170                 175
Asp Glu Met Thr Gly Tyr Val Ala Thr Arg Trp Tyr Arg Ala Pro Glu
            180                 185                 190
Ile Met Leu Asn Trp Met His Tyr Asn Gln Thr Val Asp Ile Trp Ser
        195                 200                 205
Val Gly Cys Ile Met Ala Glu Leu Leu Thr Gly Arg Thr Leu Phe Pro
    210                 215                 220
Gly Thr Asp His Ile Asp Gln Leu Lys Leu Ile Leu Arg Leu Val Gly
225                 230                 235                 240
Thr Pro Gly Ala Glu Leu Leu Lys Lys Ile Ser Ser Glu Ser Ala Arg
                245                 250                 255
Asn Tyr Ile Gln Ser Leu Thr Gln Met Pro Lys Met Asn Phe Ala Asn
            260                 265                 270
Val Phe Ile Gly Ala Asn Pro Leu Ala Val Asp Leu Leu Glu Lys Met
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        275                 280                 285
Leu Val Leu Asp Ser Asp Lys Arg Ile Thr Ala Ala Gln Ala Leu Ala
    290                 295                 300
His Ala Tyr Phe Ala Gln Tyr His Asp Pro Asp Asp Glu Pro Val Ala
305                 310                 315                 320
Asp Pro Tyr Asp Gln Ser Phe Glu Ser Arg Asp Leu Leu Ile Asp Glu
                325                 330                 335
Trp Lys Ser Leu Thr Tyr Asp Glu Val Ile Ser Phe Val Pro Pro Pro
            340                 345                 350
Leu Asp Gln Glu Glu Met Glu Ser Glu Asp Pro Pro Val Ala Thr Met
        355                 360                 365
Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val
    370                 375                 380
Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu
385                 390                 395                 400
Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys
                405                 410                 415
Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu
            420                 425                 430
Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln
        435                 440                 445
His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg
    450                 455                 460
Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val
465                 470                 475                 480
Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile
                485                 490                 495
Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn
            500                 505                 510
Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly
        515                 520                 525
Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val
    530                 535                 540
Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro
545                 550                 555                 560
Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser
                565                 570                 575
Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val
            580                 585                 590
Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
        595                 600                 605
```

(2) INFORMATION FOR SEQ ID NO:66:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2913 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...2910
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:66:

```
ATG AGT GCT GAG GGG TAC CAG TAC AGA GCG CTG TAT GAT TAT AAA AAG      48
Met Ser Ala Glu Gly Tyr Gln Tyr Arg Ala Leu Tyr Asp Tyr Lys Lys
 1               5                  10                  15

GAA AGA GAA GAA GAT ATT GAC TTG CAC TTG GGT GAC ATA TTG ACT GTG      96
Glu Arg Glu Glu Asp Ile Asp Leu His Leu Gly Asp Ile Leu Thr Val
            20                  25                  30

AAT AAA GGG TCC TTA GTA GCT CTT GGA TTC AGT GAT GGA CAG GAA GCC     144
Asn Lys Gly Ser Leu Val Ala Leu Gly Phe Ser Asp Gly Gln Glu Ala
        35                  40                  45

AGG CCT GAA GAA ATT GGC TGG TTA AAT GGC TAT AAT GAA ACC ACA GGG     192
Arg Pro Glu Glu Ile Gly Trp Leu Asn Gly Tyr Asn Glu Thr Thr Gly
    50                  55                  60

GAA AGG GGG GAC TTT CCG GGA ACT TAC GTA GAA TAT ATT GGA AGG AAA     240
Glu Arg Gly Asp Phe Pro Gly Thr Tyr Val Glu Tyr Ile Gly Arg Lys
65                  70                  75                  80

AAA ATC TCG CCT CCC ACA CCA AAG CCC CGG CCA CCT CGG CCT CTT CCT     288
Lys Ile Ser Pro Pro Thr Pro Lys Pro Arg Pro Pro Arg Pro Leu Pro
                85                  90                  95

GTT GCA CCA GGT TCT TCG AAA ACT GAA GCA GAT GTT GAA CAA CAA GCT     336
Val Ala Pro Gly Ser Ser Lys Thr Glu Ala Asp Val Glu Gln Gln Ala
            100                 105                 110

TTG ACT CTC CCG GAT CTT GCA GAG CAG TTT GCC CCT CCT GAC ATT GCC     384
Leu Thr Leu Pro Asp Leu Ala Glu Gln Phe Ala Pro Pro Asp Ile Ala
        115                 120                 125

CCG CCT CTT CTT ATC AAG CTC GTG GAA GCC ATT GAA AAG AAA GGT CTG     432
Pro Pro Leu Leu Ile Lys Leu Val Glu Ala Ile Glu Lys Lys Gly Leu
    130                 135                 140

GAA TGT TCA ACT CTA TAC AGA ACA CAG AGC TCC AGC AAC CTG GCA GAA     480
Glu Cys Ser Thr Leu Tyr Arg Thr Gln Ser Ser Ser Asn Leu Ala Glu
145                 150                 155                 160

TTA CGA CAG CTT CTT GAT TGT GAT ACA CCC TCC GTG GAC TTG GAA ATG     528
Leu Arg Gln Leu Leu Asp Cys Asp Thr Pro Ser Val Asp Leu Glu Met
                165                 170                 175

ATC GAT GTG CAC GTT TTG GCT GAC GCT TTC AAA CGC TAT CTC CTG GAC     576
Ile Asp Val His Val Leu Ala Asp Ala Phe Lys Arg Tyr Leu Leu Asp
            180                 185                 190

TTA CCA AAT CCT GTC ATT CCA GCA GCC GTT TAC AGT GAA ATG ATT TCT     624
Leu Pro Asn Pro Val Ile Pro Ala Ala Val Tyr Ser Glu Met Ile Ser
        195                 200                 205

TTA GCT CCA GAA GTA CAA AGC TCC GAA GAA TAT ATT CAG CTA TTG AAG     672
```


BNSDOCID: <WO___9845704A2_I_>

```
Leu Ala Pro Glu Val Gln Ser Ser Glu Glu Tyr Ile Gln Leu Leu Lys
    210                 215                 220

AAG CTT ATT AGG TCG CCT AGC ATA CCT CAT CAG TAT TGG CTT ACG CTT      720
Lys Leu Ile Arg Ser Pro Ser Ile Pro His Gln Tyr Trp Leu Thr Leu
225                 230                 235                 240

CAG TAT TTG TTA AAA CAT TTC TTC AAG CTC TCT CAA ACC TCC AGC AAA      768
Gln Tyr Leu Leu Lys His Phe Phe Lys Leu Ser Gln Thr Ser Ser Lys
                245                 250                 255

AAT CTG TTG AAT GCA AGA GTA CTC TCT GAA ATT TTC AGC CCT ATG CTT      816
Asn Leu Leu Asn Ala Arg Val Leu Ser Glu Ile Phe Ser Pro Met Leu
            260                 265                 270

TTC AGA TTC TCA GCA GCC AGC TCT GAT AAT ACT GAA AAC CTC ATA AAA      864
Phe Arg Phe Ser Ala Ala Ser Ser Asp Asn Thr Glu Asn Leu Ile Lys
        275                 280                 285

GTT ATA GAA ATT TTA ATC TCA ACT GAA TGG AAT GAA CGA CAG CCT GCA      912
Val Ile Glu Ile Leu Ile Ser Thr Glu Trp Asn Glu Arg Gln Pro Ala
    290                 295                 300

CCA GCA CTG CCT CCT AAA CCA CCA AAA CCT ACT ACT GTA GCC AAC AAC      960
Pro Ala Leu Pro Pro Lys Pro Pro Lys Pro Thr Thr Val Ala Asn Asn
305                 310                 315                 320

GGT ATG AAT AAC AAT ATG TCC TTA CAA AAT GCT GAA TGG TAC TGG GGA     1008
Gly Met Asn Asn Asn Met Ser Leu Gln Asn Ala Glu Trp Tyr Trp Gly
                325                 330                 335

GAT ATC TCG AGG GAA GAA GTG AAT GAA AAA CTT CGA GAT ACA GCA GAC     1056
Asp Ile Ser Arg Glu Glu Val Asn Glu Lys Leu Arg Asp Thr Ala Asp
            340                 345                 350

GGG ACC TTT TTG GTA CGA GAT GCG TCT ACT AAA ATG CAT GGT GAT TAT     1104
Gly Thr Phe Leu Val Arg Asp Ala Ser Thr Lys Met His Gly Asp Tyr
        355                 360                 365

ACT CTT ACA CTA AGG AAA GGG GGA AAT AAC AAA TTA ATC AAA ATA TTT     1152
Thr Leu Thr Leu Arg Lys Gly Gly Asn Asn Lys Leu Ile Lys Ile Phe
    370                 375                 380

CAT CGA GAT GGG AAA TAT GGC TTC TCT GAC CCA TTA ACC TTC AGT TCT     1200
His Arg Asp Gly Lys Tyr Gly Phe Ser Asp Pro Leu Thr Phe Ser Ser
385                 390                 395                 400

GTG GTT GAA TTA ATA AAC CAC TAC CGG AAT GAA TCT CTA GCT CAG TAT     1248
Val Val Glu Leu Ile Asn His Tyr Arg Asn Glu Ser Leu Ala Gln Tyr
                405                 410                 415

AAT CCC AAA TTG GAT GTG AAA TTA CTT TAT CCA GTA TCC AAA TAC CAA     1296
Asn Pro Lys Leu Asp Val Lys Leu Leu Tyr Pro Val Ser Lys Tyr Gln
            420                 425                 430

CAG GAT CAA GTT GTC AAA GAA GAT AAT ATT GAA GCT GTA GGG AAA AAA     1344
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Gln Asp Gln Val Val Lys Glu Asp Asn Ile Glu Ala Val Gly Lys Lys
        435                 440                 445

TTA CAT GAA TAT AAC ACT CAG TTT CAA GAA AAA AGT CGA GAA TAT GAT    1392
Leu His Glu Tyr Asn Thr Gln Phe Gln Glu Lys Ser Arg Glu Tyr Asp
    450                 455                 460

AGA TTA TAT GAA GAA TAT ACC CGC ACA TCC CAG GAA ATC CAA ATG AAA    1440
Arg Leu Tyr Glu Glu Tyr Thr Arg Thr Ser Gln Glu Ile Gln Met Lys
465                 470                 475                 480

AGG ACA GCT ATT GAA GCA TTT AAT GAA ACC ATA AAA ATA TTT GAA GAA    1488
Arg Thr Ala Ile Glu Ala Phe Asn Glu Thr Ile Lys Ile Phe Glu Glu
                485                 490                 495

CAG TGC CAG ACC CAA GAG CGG TAC AGC AAA GAA TAC ATA GAA AAG TTT    1536
Gln Cys Gln Thr Gln Glu Arg Tyr Ser Lys Glu Tyr Ile Glu Lys Phe
            500                 505                 510

AAA CGT GAA GGC AAT GAG AAA GAA ATA CAA AGG ATT ATG CAT AAT TAT    1584
Lys Arg Glu Gly Asn Glu Lys Glu Ile Gln Arg Ile Met His Asn Tyr
        515                 520                 525

GAT AAG TTG AAG TCT CGA ATC AGT GAA ATT ATT GAC AGT AGA AGA AGA    1632
Asp Lys Leu Lys Ser Arg Ile Ser Glu Ile Ile Asp Ser Arg Arg Arg
    530                 535                 540

TTG GAA GAA GAC TTG AAG AAG CAG GCA GCT GAG TAT CGA GAA ATT GAC    1680
Leu Glu Glu Asp Leu Lys Lys Gln Ala Ala Glu Tyr Arg Glu Ile Asp
545                 550                 555                 560

AAA CGT ATG AAC AGC ATT AAA CCA GAC CTT ATC CAG CTG AGA AAG ACG    1728
Lys Arg Met Asn Ser Ile Lys Pro Asp Leu Ile Gln Leu Arg Lys Thr
                565                 570                 575

AGA GAC CAA TAC TTG ATG TGG TTG ACT CAA AAA GGT GTT CGG CAA AAG    1776
Arg Asp Gln Tyr Leu Met Trp Leu Thr Gln Lys Gly Val Arg Gln Lys
            580                 585                 590

AAG TTG AAC GAG TGG TTG GGC AAT GAA AAC ACT GAA GAC CAA TAT TCA    1824
Lys Leu Asn Glu Trp Leu Gly Asn Glu Asn Thr Glu Asp Gln Tyr Ser
        595                 600                 605

CTG GTG GAA GAT GAT GAA GAT TTG CCC CAT CAT GAT GAG AAG ACA TGG    1872
Leu Val Glu Asp Asp Glu Asp Leu Pro His His Asp Glu Lys Thr Trp
    610                 615                 620

AAT GTT GGA AGC AGC AAC CGA AAC AAA GCT GAA AAC CTG TTG CGA GGG    1920
Asn Val Gly Ser Ser Asn Arg Asn Lys Ala Glu Asn Leu Leu Arg Gly
625                 630                 635                 640

AAG CGA GAT GGC ACT TTT CTT GTC CGG GAG AGC AGT AAA CAG GGC TGC    1968
Lys Arg Asp Gly Thr Phe Leu Val Arg Glu Ser Ser Lys Gln Gly Cys
                645                 650                 655

TAT GCC TGC TCT GTA GTG GTG GAC GGC GAA GTA AAG CAT TGT GTC ATA    2016
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Tyr Ala Cys Ser Val Val Val Asp Gly Glu Val Lys His Cys Val Ile
            660                 665                 670

AAC AAA ACA GCA ACT GGC TAT GGC TTT GCC GAG CCC TAT AAC TTG TAC    2064
Asn Lys Thr Ala Thr Gly Tyr Gly Phe Ala Glu Pro Tyr Asn Leu Tyr
        675                 680                 685

AGC TCT CTG AAA GAA CTG GTG CTA CAT TAC CAA CAC ACC TCC CTT GTG    2112
Ser Ser Leu Lys Glu Leu Val Leu His Tyr Gln His Thr Ser Leu Val
    690                 695                 700

CAG CAC AAC GAC TCC CTC AAT GTC ACA CTA GCC TAC CCA GTA TAT GCA    2160
Gln His Asn Asp Ser Leu Asn Val Thr Leu Ala Tyr Pro Val Tyr Ala
705                 710                 715                 720

CAG CAG AGG CGA CAG GAT CCA CCG GTC GCC ACC ATG GTG AGC AAG GGC    2208
Gln Gln Arg Arg Gln Asp Pro Pro Val Ala Thr Met Val Ser Lys Gly
                725                 730                 735

GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG GTC GAG CTG GAC GGC    2256
Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly
            740                 745                 750

GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC GAG GGC GAG GGC GAT    2304
Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp
        755                 760                 765

GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC TGC ACC ACC GGC AAG    2352
Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys
    770                 775                 780

CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC CTG ACC TAC GGC GTG    2400
Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Thr Tyr Gly Val
785                 790                 795                 800

CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG CAG CAC GAC TTC TTC    2448
Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln His Asp Phe Phe
                805                 810                 815

AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG CGC ACC ATC TTC TTC    2496
Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe
            820                 825                 830

AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG GTG AAG TTC GAG GGC    2544
Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly
        835                 840                 845

GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC ATC GAC TTC AAG GAG    2592
Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu
    850                 855                 860

GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC AAC TAC AAC AGC CAC    2640
Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His
865                 870                 875                 880

AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC GGC ATC AAG GTG AAC    2688
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Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn
                885                 890                 895

TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC GTG CAG CTC GCC GAC    2736
Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp
            900                 905                 910

CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC CCC GTG CTG CTG CCC    2784
His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro
        915                 920                 925

GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG AGC AAA GAC CCC AAC    2832
Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn
    930                 935                 940

GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC GTG ACC GCC GCC GGG    2880
Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly
945                 950                 955                 960

ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TAA                        2913
Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
                965                 970
```

(2) INFORMATION FOR SEQ ID NO:67:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 970 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:67:

```
Met Ser Ala Glu Gly Tyr Gln Tyr Arg Ala Leu Tyr Asp Tyr Lys Lys
 1               5                  10                  15
Glu Arg Glu Glu Asp Ile Asp Leu His Leu Gly Asp Ile Leu Thr Val
            20                  25                  30
Asn Lys Gly Ser Leu Val Ala Leu Gly Phe Ser Asp Gly Gln Glu Ala
        35                  40                  45
Arg Pro Glu Glu Ile Gly Trp Leu Asn Gly Tyr Asn Glu Thr Thr Gly
    50                  55                  60
Glu Arg Gly Asp Phe Pro Gly Thr Tyr Val Glu Tyr Ile Gly Arg Lys
65                  70                  75                  80
Lys Ile Ser Pro Pro Thr Pro Lys Pro Arg Pro Pro Arg Pro Leu Pro
                85                  90                  95
Val Ala Pro Gly Ser Ser Lys Thr Glu Ala Asp Val Glu Gln Gln Ala
            100                 105                 110
Leu Thr Leu Pro Asp Leu Ala Glu Gln Phe Ala Pro Pro Asp Ile Ala
        115                 120                 125
Pro Pro Leu Leu Ile Lys Leu Val Glu Ala Ile Glu Lys Lys Gly Leu
    130                 135                 140
Glu Cys Ser Thr Leu Tyr Arg Thr Gln Ser Ser Ser Asn Leu Ala Glu
```

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145                 150                 155                 160
Leu Arg Gln Leu Leu Asp Cys Asp Thr Pro Ser Val Asp Leu Glu Met
                165                 170                 175
Ile Asp Val His Val Leu Ala Asp Ala Phe Lys Arg Tyr Leu Leu Asp
            180                 185                 190
Leu Pro Asn Pro Val Ile Pro Ala Ala Val Tyr Ser Glu Met Ile Ser
        195                 200                 205
Leu Ala Pro Glu Val Gln Ser Ser Glu Glu Tyr Ile Gln Leu Leu Lys
    210                 215                 220
Lys Leu Ile Arg Ser Pro Ser Ile Pro His Gln Tyr Trp Leu Thr Leu
225                 230                 235                 240
Gln Tyr Leu Leu Lys His Phe Phe Lys Leu Ser Gln Thr Ser Ser Lys
                245                 250                 255
Asn Leu Leu Asn Ala Arg Val Leu Ser Glu Ile Phe Ser Pro Met Leu
            260                 265                 270
Phe Arg Phe Ser Ala Ala Ser Ser Asp Asn Thr Glu Asn Leu Ile Lys
        275                 280                 285
Val Ile Glu Ile Leu Ile Ser Thr Glu Trp Asn Glu Arg Gln Pro Ala
    290                 295                 300
Pro Ala Leu Pro Pro Lys Pro Pro Lys Pro Thr Thr Val Ala Asn Asn
305                 310                 315                 320
Gly Met Asn Asn Asn Met Ser Leu Gln Asn Ala Glu Trp Tyr Trp Gly
                325                 330                 335
Asp Ile Ser Arg Glu Glu Val Asn Glu Lys Leu Arg Asp Thr Ala Asp
            340                 345                 350
Gly Thr Phe Leu Val Arg Asp Ala Ser Thr Lys Met His Gly Asp Tyr
        355                 360                 365
Thr Leu Thr Leu Arg Lys Gly Gly Asn Asn Lys Leu Ile Lys Ile Phe
    370                 375                 380
His Arg Asp Gly Lys Tyr Gly Phe Ser Asp Pro Leu Thr Phe Ser Ser
385                 390                 395                 400
Val Val Glu Leu Ile Asn His Tyr Arg Asn Glu Ser Leu Ala Gln Tyr
                405                 410                 415
Asn Pro Lys Leu Asp Val Lys Leu Leu Tyr Pro Val Ser Lys Tyr Gln
            420                 425                 430
Gln Asp Gln Val Val Lys Glu Asp Asn Ile Glu Ala Val Gly Lys Lys
        435                 440                 445
Leu His Glu Tyr Asn Thr Gln Phe Gln Glu Lys Ser Arg Glu Tyr Asp
    450                 455                 460
Arg Leu Tyr Glu Glu Tyr Thr Arg Thr Ser Gln Glu Ile Gln Met Lys
465                 470                 475                 480
Arg Thr Ala Ile Glu Ala Phe Asn Glu Thr Ile Lys Ile Phe Glu Glu
                485                 490                 495
Gln Cys Gln Thr Gln Glu Arg Tyr Ser Lys Glu Tyr Ile Glu Lys Phe
            500                 505                 510
Lys Arg Glu Gly Asn Glu Lys Glu Ile Gln Arg Ile Met His Asn Tyr
        515                 520                 525
Asp Lys Leu Lys Ser Arg Ile Ser Glu Ile Ile Asp Ser Arg Arg Arg
    530                 535                 540
Leu Glu Glu Asp Leu Lys Lys Gln Ala Ala Glu Tyr Arg Glu Ile Asp
545                 550                 555                 560
Lys Arg Met Asn Ser Ile Lys Pro Asp Leu Ile Gln Leu Arg Lys Thr
                565                 570                 575
Arg Asp Gln Tyr Leu Met Trp Leu Thr Gln Lys Gly Val Arg Gln Lys
            580                 585                 590
Lys Leu Asn Glu Trp Leu Gly Asn Glu Asn Thr Glu Asp Gln Tyr Ser
```

595 600 605
Leu Val Glu Asp Asp Glu Asp Leu Pro His His Asp Glu Lys Thr Trp
610 615 620
Asn Val Gly Ser Ser Asn Arg Asn Lys Ala Glu Asn Leu Leu Arg Gly
625 630 635 640
Lys Arg Asp Gly Thr Phe Leu Val Arg Glu Ser Ser Lys Gln Gly Cys
645 650 655
Tyr Ala Cys Ser Val Val Val Asp Gly Glu Val Lys His Cys Val Ile
660 665 670
Asn Lys Thr Ala Thr Gly Tyr Gly Phe Ala Glu Pro Tyr Asn Leu Tyr
675 680 685
Ser Ser Leu Lys Glu Leu Val Leu His Tyr Gln His Thr Ser Leu Val
690 695 700
Gln His Asn Asp Ser Leu Asn Val Thr Leu Ala Tyr Pro Val Tyr Ala
705 710 715 720
Gln Gln Arg Arg Gln Asp Pro Pro Val Ala Thr Met Val Ser Lys Gly
725 730 735
Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly
740 745 750
Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp
755 760 765
Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys
770 775 780
Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Thr Tyr Gly Val
785 790 795 800
Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln His Asp Phe Phe
805 810 815
Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe
820 825 830
Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly
835 840 845
Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu
850 855 860
Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His
865 870 875 880
Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn
885 890 895
Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp
900 905 910
His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro
915 920 925
Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn
930 935 940
Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly
945 950 955 960
Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
965 970

(2) INFORMATION FOR SEQ ID NO:68:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1788 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

BNSDOCID: <WO__9845704A2_I_>

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...1785
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:68:

```
ATG GGC AAC GCC GCC GCC GCC AAG AAG GGC AGC GAG CAG GAG AGC GTG      48
Met Gly Asn Ala Ala Ala Ala Lys Lys Gly Ser Glu Gln Glu Ser Val
 1               5                  10                  15

AAA GAG TTC CTA GCC AAA GCC AAG GAA GAT TTC CTG AAA AAA TGG GAA      96
Lys Glu Phe Leu Ala Lys Ala Lys Glu Asp Phe Leu Lys Lys Trp Glu
            20                  25                  30

GAC CCC TCT CAG AAT ACA GCC CAG TTG GAT CAG TTT GAT AGA ATC AAG     144
Asp Pro Ser Gln Asn Thr Ala Gln Leu Asp Gln Phe Asp Arg Ile Lys
        35                  40                  45

ACC CTT GGC ACC GGC TCC TTT GGG CGA GTG ATG CTG GTG AAG CAC AAG     192
Thr Leu Gly Thr Gly Ser Phe Gly Arg Val Met Leu Val Lys His Lys
    50                  55                  60

GAG AGT GGG AAC CAC TAC GCC ATG AAG ATC TTA GAC AAG CAG AAG GTG     240
Glu Ser Gly Asn His Tyr Ala Met Lys Ile Leu Asp Lys Gln Lys Val
65                  70                  75                  80

GTG AAG CTA AAG CAG ATC GAG CAC ACT CTG AAT GAG AAG CGC ATC CTG     288
Val Lys Leu Lys Gln Ile Glu His Thr Leu Asn Glu Lys Arg Ile Leu
                85                  90                  95

CAG GCC GTC AAC TTC CCG TTC CTG GTC AAA CTT GAA TTC TCC TTC AAG     336
Gln Ala Val Asn Phe Pro Phe Leu Val Lys Leu Glu Phe Ser Phe Lys
            100                 105                 110

GAC AAC TCA AAC CTG TAC ATG GTC ATG GAG TAT GTA GCT GGT GGC GAG     384
Asp Asn Ser Asn Leu Tyr Met Val Met Glu Tyr Val Ala Gly Gly Glu
        115                 120                 125

ATG TTC TCC CAC CTA CGG CGG ATT GGA AGG TTC AGC GAG CCC CAT GCC     432
Met Phe Ser His Leu Arg Arg Ile Gly Arg Phe Ser Glu Pro His Ala
    130                 135                 140

CGT TTC TAC GCG GCG CAG ATC GTC CTG ACC TTT GAG TAT CTG CAC TCC     480
Arg Phe Tyr Ala Ala Gln Ile Val Leu Thr Phe Glu Tyr Leu His Ser
145                 150                 155                 160

CTG GAC CTC ATC TAC CGG GAC CTG AAG CCC GAG AAT CTT CTC ATC GAC     528
Leu Asp Leu Ile Tyr Arg Asp Leu Lys Pro Glu Asn Leu Leu Ile Asp
                165                 170                 175

CAG CAG GGC TAT ATT CAG GTG ACA GAC TTC GGT TTT GCC AAG CGT GTG     576
Gln Gln Gly Tyr Ile Gln Val Thr Asp Phe Gly Phe Ala Lys Arg Val
            180                 185                 190
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BNSDOCID: <WO__9845704A2_I_>

```
AAA GGC CGT ACT TGG ACC TTG TGT GGG ACC CCT GAG TAC TTG GCC CCC      624
Lys Gly Arg Thr Trp Thr Leu Cys Gly Thr Pro Glu Tyr Leu Ala Pro
        195                 200                 205

GAG ATT ATC CTG AGC AAA GGC TAC AAC AAG GCT GTG GAC TGG TGG GCT      672
Glu Ile Ile Leu Ser Lys Gly Tyr Asn Lys Ala Val Asp Trp Trp Ala
    210                 215                 220

CTC GGA GTC CTC ATC TAC GAG ATG GCT GCT GGT TAC CCA CCC TTC TTC      720
Leu Gly Val Leu Ile Tyr Glu Met Ala Ala Gly Tyr Pro Pro Phe Phe
225                 230                 235                 240

GCT GAC CAG CCT ATC CAG ATC TAT GAG AAA ATC GTC TCT GGG AAG GTG      768
Ala Asp Gln Pro Ile Gln Ile Tyr Glu Lys Ile Val Ser Gly Lys Val
                245                 250                 255

CGG TTC CCA TCC CAC TTC AGC TCT GAC TTG AAG GAC CTG CTG CGG AAC      816
Arg Phe Pro Ser His Phe Ser Ser Asp Leu Lys Asp Leu Leu Arg Asn
            260                 265                 270

CTT CTG CAA GTG GAT CTA ACC AAG CGC TTT GGA AAC CTC AAG GAC GGG      864
Leu Leu Gln Val Asp Leu Thr Lys Arg Phe Gly Asn Leu Lys Asp Gly
        275                 280                 285

GTC AAT GAC ATC AAG AAC CAC AAG TGG TTT GCC ACG ACT GAC TGG ATT      912
Val Asn Asp Ile Lys Asn His Lys Trp Phe Ala Thr Thr Asp Trp Ile
    290                 295                 300

GCC ATC TAT CAG AGA AAG GTG GAA GCT CCC TTC ATA CCA AAG TTT AAA      960
Ala Ile Tyr Gln Arg Lys Val Glu Ala Pro Phe Ile Pro Lys Phe Lys
305                 310                 315                 320

GGC CCT GGG GAC ACG AGT AAC TTT GAC GAC TAT GAG GAG GAA GAG ATC     1008
Gly Pro Gly Asp Thr Ser Asn Phe Asp Asp Tyr Glu Glu Glu Glu Ile
                325                 330                 335

CGG GTC TCC ATC AAT GAG AAG TGT GGC AAG GAG TTT ACT GAG TTT GGG     1056
Arg Val Ser Ile Asn Glu Lys Cys Gly Lys Glu Phe Thr Glu Phe Gly
            340                 345                 350

CGC GCC ATG AGT AAA GGA GAA GAA CTT TTC ACT GGA GTT GTC CCA ATT     1104
Arg Ala Met Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile
        355                 360                 365

CTT GTT GAA TTA GAT GGC GAT GTT AAT GGG CAA AAA TTC TCT GTT AGT     1152
Leu Val Glu Leu Asp Gly Asp Val Asn Gly Gln Lys Phe Ser Val Ser
    370                 375                 380

GGA GAG GGT GAA GGT GAT GCA ACA TAC GGA AAA CTT ACC CTT AAA TTT     1200
Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe
385                 390                 395                 400

ATT TGC ACT ACT GGG AAG CTA CCT GTT CCA TGG CCA ACG CTT GTC ACT     1248
Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr
                405                 410                 415
```

ACT CTC ACT TAT GGT GTT CAA TGC TTT TCT AGA TAC CCA GAT CAT ATG 1296
Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met
420 425 430

AAA CAG CAT GAC TTT TTC AAG AGT GCC ATG CCC GAA GGT TAT GTA CAG 1344
Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln
435 440 445

GAA AGA ACT ATA TTT TAC AAA GAT GAC GGG AAC TAC AAG ACA CGT GCT 1392
Glu Arg Thr Ile Phe Tyr Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala
450 455 460

GAA GTC AAG TTT GAA GGT GAT ACC CTT GTT AAT AGA ATC GAG TTA AAA 1440
Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys
465 470 475 480

GGT ATT GAT TTT AAA GAA GAT GGA AAC ATT CTT GGA CAC AAA ATG GAA 1488
Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Met Glu
485 490 495

TAC AAT TAT AAC TCA CAT AAT GTA TAC ATC ATG GCA GAC AAA CCA AAG 1536
Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Pro Lys
500 505 510

AAT GGC ATC AAA GTT AAC TTC AAA ATT AGA CAC AAC ATT AAA GAT GGA 1584
Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Lys Asp Gly
515 520 525

AGC GTT CAA TTA GCA GAC CAT TAT CAA CAA AAT ACT CCA ATT GGC GAT 1632
Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp
530 535 540

GGC CCT GTC CTT TTA CCA GAC AAC CAT TAC CTG TCC ACG CAA TCT GCC 1680
Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala
545 550 555 560

CTT TCC AAA GAT CCC AAC GAA AAG AGA GAT CAC ATG ATC CTT CTT GAG 1728
Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Ile Leu Leu Glu
565 570 575

TTT GTA ACA GCT GCT GGG ATT ACA CAT GGC ATG GAT GAA CTA TAC AAA 1776
Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Lys
580 585 590

CCT CAG GAG TAA 1788
Pro Gln Glu
595

(2) INFORMATION FOR SEQ ID NO:69:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 595 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:69:

```
Met Gly Asn Ala Ala Ala Ala Lys Lys Gly Ser Glu Gln Glu Ser Val
 1               5                  10                  15
Lys Glu Phe Leu Ala Lys Ala Lys Glu Asp Phe Leu Lys Lys Trp Glu
            20                  25                  30
Asp Pro Ser Gln Asn Thr Ala Gln Leu Asp Gln Phe Asp Arg Ile Lys
        35                  40                  45
Thr Leu Gly Thr Gly Ser Phe Gly Arg Val Met Leu Val Lys His Lys
    50                  55                  60
Glu Ser Gly Asn His Tyr Ala Met Lys Ile Leu Asp Lys Gln Lys Val
65                  70                  75                  80
Val Lys Leu Lys Gln Ile Glu His Thr Leu Asn Glu Lys Arg Ile Leu
                85                  90                  95
Gln Ala Val Asn Phe Pro Phe Leu Val Lys Leu Glu Phe Ser Phe Lys
            100                 105                 110
Asp Asn Ser Asn Leu Tyr Met Val Met Glu Tyr Val Ala Gly Gly Glu
        115                 120                 125
Met Phe Ser His Leu Arg Arg Ile Gly Arg Phe Ser Glu Pro His Ala
    130                 135                 140
Arg Phe Tyr Ala Ala Gln Ile Val Leu Thr Phe Glu Tyr Leu His Ser
145                 150                 155                 160
Leu Asp Leu Ile Tyr Arg Asp Leu Lys Pro Glu Asn Leu Leu Ile Asp
                165                 170                 175
Gln Gln Gly Tyr Ile Gln Val Thr Asp Phe Gly Phe Ala Lys Arg Val
            180                 185                 190
Lys Gly Arg Thr Trp Thr Leu Cys Gly Thr Pro Glu Tyr Leu Ala Pro
        195                 200                 205
Glu Ile Ile Leu Ser Lys Gly Tyr Asn Lys Ala Val Asp Trp Trp Ala
    210                 215                 220
Leu Gly Val Leu Ile Tyr Glu Met Ala Ala Gly Tyr Pro Pro Phe Phe
225                 230                 235                 240
Ala Asp Gln Pro Ile Gln Ile Tyr Glu Lys Ile Val Ser Gly Lys Val
                245                 250                 255
Arg Phe Pro Ser His Phe Ser Ser Asp Leu Lys Asp Leu Leu Arg Asn
            260                 265                 270
Leu Leu Gln Val Asp Leu Thr Lys Arg Phe Gly Asn Leu Lys Asp Gly
        275                 280                 285
Val Asn Asp Ile Lys Asn His Lys Trp Phe Ala Thr Thr Asp Trp Ile
    290                 295                 300
Ala Ile Tyr Gln Arg Lys Val Glu Ala Pro Phe Ile Pro Lys Phe Lys
305                 310                 315                 320
Gly Pro Gly Asp Thr Ser Asn Phe Asp Asp Tyr Glu Glu Glu Glu Ile
                325                 330                 335
Arg Val Ser Ile Asn Glu Lys Cys Gly Lys Glu Phe Thr Glu Phe Gly
            340                 345                 350
Arg Ala Met Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile
        355                 360                 365
Leu Val Glu Leu Asp Gly Asp Val Asn Gly Gln Lys Phe Ser Val Ser
    370                 375                 380
Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe
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385                 390                 395                 400
Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr
                405                 410                 415
Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met
            420                 425                 430
Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln
        435                 440                 445
Glu Arg Thr Ile Phe Tyr Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala
    450                 455                 460
Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys
465                 470                 475                 480
Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Met Glu
                485                 490                 495
Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Pro Lys
            500                 505                 510
Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Lys Asp Gly
        515                 520                 525
Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp
    530                 535                 540
Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala
545                 550                 555                 560
Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Ile Leu Leu Glu
                565                 570                 575
Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Lys
            580                 585                 590
Pro Gln Glu
        595
```

(2) INFORMATION FOR SEQ ID NO:70:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2181 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...2178
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:70:

```
ATG AGC GAC GTG GCT ATT GTG AAG GAG GGT TGG CTG CAC AAA CGA GGG      48
Met Ser Asp Val Ala Ile Val Lys Glu Gly Trp Leu His Lys Arg Gly
 1               5                  10                  15

GAG TAC ATC AAG ACC TGG CGG CCA CGC TAC TTC CTC CTC AAG AAT GAT      96
Glu Tyr Ile Lys Thr Trp Arg Pro Arg Tyr Phe Leu Leu Lys Asn Asp
            20                  25                  30

GGC ACC TTC ATT GGC TAC AAG GAG CGG CCG CAG GAT GTG GAC CAA CGT     144
Gly Thr Phe Ile Gly Tyr Lys Glu Arg Pro Gln Asp Val Asp Gln Arg
        35                  40                  45
```

```
GAG GCT CCC CTC AAC AAC TTC TCT GTG GCG CAG TGC CAG CTG ATG AAG     192
Glu Ala Pro Leu Asn Asn Phe Ser Val Ala Gln Cys Gln Leu Met Lys
    50                  55                  60

ACG GAG CGG CCC CGG CCC AAC ACC TTC ATC ATC CGC TGC CTG CAG TGG     240
Thr Glu Arg Pro Arg Pro Asn Thr Phe Ile Ile Arg Cys Leu Gln Trp
65                  70                  75                  80

ACC ACT GTC ATC GAA CGC ACC TTC CAT GTG GAG ACT CCT GAG GAG CGG     288
Thr Thr Val Ile Glu Arg Thr Phe His Val Glu Thr Pro Glu Glu Arg
                85                  90                  95

GAG GAG TGG ACA ACC GCC ATC CAG ACT GTG GCT GAC GGC CTC AAG AAG     336
Glu Glu Trp Thr Thr Ala Ile Gln Thr Val Ala Asp Gly Leu Lys Lys
            100                 105                 110

CAG GAG GAG GAG GAG ATG GAC TTC CGG TCG GGC TCA CCC AGT GAC AAC     384
Gln Glu Glu Glu Glu Met Asp Phe Arg Ser Gly Ser Pro Ser Asp Asn
        115                 120                 125

TCA GGG GCT GAA GAG ATG GAG GTG TCC CTG GCC AAG CCC AAG CAC CGC     432
Ser Gly Ala Glu Glu Met Glu Val Ser Leu Ala Lys Pro Lys His Arg
    130                 135                 140

GTG ACC ATG AAC GAG TTT GAG TAC CTG AAG CTG CTG GGC AAG GGC ACT     480
Val Thr Met Asn Glu Phe Glu Tyr Leu Lys Leu Leu Gly Lys Gly Thr
145                 150                 155                 160

TTC GGC AAG GTG ATC CTG GTG AAG GAG AAG GCC ACA GGC CGC TAC TAC     528
Phe Gly Lys Val Ile Leu Val Lys Glu Lys Ala Thr Gly Arg Tyr Tyr
                165                 170                 175

GCC ATG AAG ATC CTC AAG AAG GAA GTC ATC GTG GCC AAG GAC GAG GTG     576
Ala Met Lys Ile Leu Lys Lys Glu Val Ile Val Ala Lys Asp Glu Val
            180                 185                 190

GCC CAC ACA CTC ACC GAG AAC CGC GTC CTG CAG AAC TCC AGG CAC CCC     624
Ala His Thr Leu Thr Glu Asn Arg Val Leu Gln Asn Ser Arg His Pro
        195                 200                 205

TTC CTC ACA GCC CTG AAG TAC TCT TTC CAG ACC CAC GAC CGC CTC TGC     672
Phe Leu Thr Ala Leu Lys Tyr Ser Phe Gln Thr His Asp Arg Leu Cys
    210                 215                 220

TTT GTC ATG GAG TAC GCC AAC GGG GGC GAG CTG TTC TTC CAC CTG TCC     720
Phe Val Met Glu Tyr Ala Asn Gly Gly Glu Leu Phe Phe His Leu Ser
225                 230                 235                 240

CGG GAA CGT GTG TTC TCC GAG GAC CGG GCC CGC TTC TAT GGC GCT GAG     768
Arg Glu Arg Val Phe Ser Glu Asp Arg Ala Arg Phe Tyr Gly Ala Glu
                245                 250                 255

ATT GTG TCA GCC CTG GAC TAC CTG CAC TCG GAG AAG AAC GTG GTG TAC     816
Ile Val Ser Ala Leu Asp Tyr Leu His Ser Glu Lys Asn Val Val Tyr
            260                 265                 270
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CGG GAC CTC AAG CTG GAG AAC CTC ATG CTG GAC AAG GAC GGG CAC ATT      864
Arg Asp Leu Lys Leu Glu Asn Leu Met Leu Asp Lys Asp Gly His Ile
        275                 280                 285

AAG ATC ACA GAC TTC GGG CTG TGC AAG GAG GGG ATC AAG GAC GGT GCC      912
Lys Ile Thr Asp Phe Gly Leu Cys Lys Glu Gly Ile Lys Asp Gly Ala
    290                 295                 300

ACC ATG AAG ACC TTT TGC GGC ACA CCT GAG TAC CTG GCC CCC GAG GTG      960
Thr Met Lys Thr Phe Cys Gly Thr Pro Glu Tyr Leu Ala Pro Glu Val
305                 310                 315                 320

CTG GAG GAC AAT GAC TAC GGC CGT GCA GTG GAC TGG TGG GGG CTG GGC     1008
Leu Glu Asp Asn Asp Tyr Gly Arg Ala Val Asp Trp Trp Gly Leu Gly
                325                 330                 335

GTG GTC ATG TAC GAG ATG ATG TGC GGT CGC CTG CCC TTC TAC AAC CAG     1056
Val Val Met Tyr Glu Met Met Cys Gly Arg Leu Pro Phe Tyr Asn Gln
            340                 345                 350

GAC CAT GAG AAG CTT TTT GAG CTC ATC CTC ATG GAG GAG ATC CGC TTC     1104
Asp His Glu Lys Leu Phe Glu Leu Ile Leu Met Glu Glu Ile Arg Phe
        355                 360                 365

CCG CGC ACG CTT GGT CCC GAG GCC AAG TCC TTG CTT TCA GGG CTG CTC     1152
Pro Arg Thr Leu Gly Pro Glu Ala Lys Ser Leu Leu Ser Gly Leu Leu
    370                 375                 380

AAG AAG GAC CCC AAG CAG AGG CTT GGC GGG GGC TCC GAG GAC GCC AAG     1200
Lys Lys Asp Pro Lys Gln Arg Leu Gly Gly Gly Ser Glu Asp Ala Lys
385                 390                 395                 400

GAG ATC ATG CAG CAT CGC TTC TTT GCC GGT ATC GTG TGG CAG CAC GTG     1248
Glu Ile Met Gln His Arg Phe Phe Ala Gly Ile Val Trp Gln His Val
                405                 410                 415

TAC GAG AAG AAG CTC AGC CCA CCC TTC AAG CCC CAG GTC ACG TCG GAG     1296
Tyr Glu Lys Lys Leu Ser Pro Pro Phe Lys Pro Gln Val Thr Ser Glu
            420                 425                 430

ACT GAC ACC AGG TAT TTT GAT GAG GAG TTC ACG GCC CAG ATG ATC ACC     1344
Thr Asp Thr Arg Tyr Phe Asp Glu Glu Phe Thr Ala Gln Met Ile Thr
        435                 440                 445

ATC ACA CCA CCT GAC CAA GAT GAC AGC ATG GAG TGT GTG GAC AGC GAG     1392
Ile Thr Pro Pro Asp Gln Asp Asp Ser Met Glu Cys Val Asp Ser Glu
    450                 455                 460

CGC AGG CCC CAC TTC CCC CAG TTC TCC TAC TCG GCC AGC AGC ACG GCC     1440
Arg Arg Pro His Phe Pro Gln Phe Ser Tyr Ser Ala Ser Ser Thr Ala
465                 470                 475                 480

TCG GAT CCA CCG GTC GCC ACC ATG GTG AGC AAG GGC GAG GAG CTG TTC     1488
Ser Asp Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe
                485                 490                 495
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ACC GGG GTG GTG CCC ATC CTG GTC GAG CTG GAC GGC GAC GTA AAC GGC    1536
Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly
            500                 505                 510

CAC AAG TTC AGC GTG TCC GGC GAG GGC GAG GGC GAT GCC ACC TAC GGC    1584
His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly
        515                 520                 525

AAG CTG ACC CTG AAG TTC ATC TGC ACC ACC GGC AAG CTG CCC GTG CCC    1632
Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro
    530                 535                 540

TGG CCC ACC CTC GTG ACC ACC CTG ACC TAC GGC GTG CAG TGC TTC AGC    1680
Trp Pro Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser
545                 550                 555                 560

CGC TAC CCC GAC CAC ATG AAG CAG CAC GAC TTC TTC AAG TCC GCC ATG    1728
Arg Tyr Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met
                565                 570                 575

CCC GAA GGC TAC GTC CAG GAG CGC ACC ATC TTC TTC AAG GAC GAC GGC    1776
Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly
            580                 585                 590

AAC TAC AAG ACC CGC GCC GAG GTG AAG TTC GAG GGC GAC ACC CTG GTG    1824
Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val
        595                 600                 605

AAC CGC ATC GAG CTG AAG GGC ATC GAC TTC AAG GAG GAC GGC AAC ATC    1872
Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile
    610                 615                 620

CTG GGG CAC AAG CTG GAG TAC AAC TAC AAC AGC CAC AAC GTC TAT ATC    1920
Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile
625                 630                 635                 640

ATG GCC GAC AAG CAG AAG AAC GGC ATC AAG GTG AAC TTC AAG ATC CGC    1968
Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg
                645                 650                 655

CAC AAC ATC GAG GAC GGC AGC GTG CAG CTC GCC GAC CAC TAC CAG CAG    2016
His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln
            660                 665                 670

AAC ACC CCC ATC GGC GAC GGC CCC GTG CTG CTG CCC GAC AAC CAC TAC    2064
Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr
        675                 680                 685

CTG AGC ACC CAG TCC GCC CTG AGC AAA GAC CCC AAC GAG AAG CGC GAT    2112
Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp
    690                 695                 700

CAC ATG GTC CTG CTG GAG TTC GTG ACC GCC GCC GGG ATC ACT CTC GGC    2160
His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly
705                 710                 715                 720
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BNSDOCID: <WO___9845704A2_I_>

ATG GAC GAG CTG TAC AAG TAA
Met Asp Glu Leu Tyr Lys
725 2181

(2) INFORMATION FOR SEQ ID NO:71:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 726 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:71:

Met Ser Asp Val Ala Ile Val Lys Glu Gly Trp Leu His Lys Arg Gly
1 5 10 15
Glu Tyr Ile Lys Thr Trp Arg Pro Arg Tyr Phe Leu Leu Lys Asn Asp
20 25 30
Gly Thr Phe Ile Gly Tyr Lys Glu Arg Pro Gln Asp Val Asp Gln Arg
35 40 45
Glu Ala Pro Leu Asn Asn Phe Ser Val Ala Gln Cys Gln Leu Met Lys
50 55 60
Thr Glu Arg Pro Arg Pro Asn Thr Phe Ile Ile Arg Cys Leu Gln Trp
65 70 75 80
Thr Thr Val Ile Glu Arg Thr Phe His Val Glu Thr Pro Glu Glu Arg
85 90 95
Glu Glu Trp Thr Thr Ala Ile Gln Thr Val Ala Asp Gly Leu Lys Lys
100 105 110
Gln Glu Glu Glu Glu Met Asp Phe Arg Ser Gly Ser Pro Ser Asp Asn
115 120 125
Ser Gly Ala Glu Glu Met Glu Val Ser Leu Ala Lys Pro Lys His Arg
130 135 140
Val Thr Met Asn Glu Phe Glu Tyr Leu Lys Leu Leu Gly Lys Gly Thr
145 150 155 160
Phe Gly Lys Val Ile Leu Val Lys Glu Lys Ala Thr Gly Arg Tyr Tyr
165 170 175
Ala Met Lys Ile Leu Lys Lys Glu Val Ile Val Ala Lys Asp Glu Val
180 185 190
Ala His Thr Leu Thr Glu Asn Arg Val Leu Gln Asn Ser Arg His Pro
195 200 205
Phe Leu Thr Ala Leu Lys Tyr Ser Phe Gln Thr His Asp Arg Leu Cys
210 215 220
Phe Val Met Glu Tyr Ala Asn Gly Gly Glu Leu Phe Phe His Leu Ser
225 230 235 240
Arg Glu Arg Val Phe Ser Glu Asp Arg Ala Arg Phe Tyr Gly Ala Glu
245 250 255
Ile Val Ser Ala Leu Asp Tyr Leu His Ser Glu Lys Asn Val Val Tyr
260 265 270
Arg Asp Leu Lys Leu Glu Asn Leu Met Leu Asp Lys Asp Gly His Ile
275 280 285
Lys Ile Thr Asp Phe Gly Leu Cys Lys Glu Gly Ile Lys Asp Gly Ala

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    290                 295                 300
Thr Met Lys Thr Phe Cys Gly Thr Pro Glu Tyr Leu Ala Pro Glu Val
305                 310                 315                 320
Leu Glu Asp Asn Asp Tyr Gly Arg Ala Val Asp Trp Trp Gly Leu Gly
                325                 330                 335
Val Val Met Tyr Glu Met Met Cys Gly Arg Leu Pro Phe Tyr Asn Gln
            340                 345                 350
Asp His Glu Lys Leu Phe Glu Leu Ile Leu Met Glu Glu Ile Arg Phe
        355                 360                 365
Pro Arg Thr Leu Gly Pro Glu Ala Lys Ser Leu Leu Ser Gly Leu Leu
    370                 375                 380
Lys Lys Asp Pro Lys Gln Arg Leu Gly Gly Gly Ser Glu Asp Ala Lys
385                 390                 395                 400
Glu Ile Met Gln His Arg Phe Phe Ala Gly Ile Val Trp Gln His Val
                405                 410                 415
Tyr Glu Lys Lys Leu Ser Pro Pro Phe Lys Pro Gln Val Thr Ser Glu
            420                 425                 430
Thr Asp Thr Arg Tyr Phe Asp Glu Glu Phe Thr Ala Gln Met Ile Thr
        435                 440                 445
Ile Thr Pro Pro Asp Gln Asp Asp Ser Met Glu Cys Val Asp Ser Glu
    450                 455                 460
Arg Arg Pro His Phe Pro Gln Phe Ser Tyr Ser Ala Ser Ser Thr Ala
465                 470                 475                 480
Ser Asp Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe
                485                 490                 495
Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly
            500                 505                 510
His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly
        515                 520                 525
Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro
    530                 535                 540
Trp Pro Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser
545                 550                 555                 560
Arg Tyr Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met
                565                 570                 575
Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly
            580                 585                 590
Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val
        595                 600                 605
Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile
    610                 615                 620
Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile
625                 630                 635                 640
Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg
                645                 650                 655
His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln
            660                 665                 670
Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr
        675                 680                 685
Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp
    690                 695                 700
His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly
705                 710                 715                 720
Met Asp Glu Leu Tyr Lys
                725
```

(2) INFORMATION FOR SEQ ID NO:72:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2751 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...2748
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:72:

```
ATG GCT GAC GTT TAC CCG GCC AAC GAC TCC ACG GCG TCT CAG GAC GTG      48
Met Ala Asp Val Tyr Pro Ala Asn Asp Ser Thr Ala Ser Gln Asp Val
 1               5                  10                  15

GCC AAC CGC TTC GCC CGC AAA GGG GCG CTG AGG CAG AAG AAC GTG CAT      96
Ala Asn Arg Phe Ala Arg Lys Gly Ala Leu Arg Gln Lys Asn Val His
            20                  25                  30

GAG GTG AAA GAC CAC AAA TTC ATC GCC CGC TTC TTC AAG CAA CCC ACC     144
Glu Val Lys Asp His Lys Phe Ile Ala Arg Phe Phe Lys Gln Pro Thr
        35                  40                  45

TTC TGC AGC CAC TGC ACC GAC TTC ATC TGG GGG TTT GGG AAA CAA GGC     192
Phe Cys Ser His Cys Thr Asp Phe Ile Trp Gly Phe Gly Lys Gln Gly
    50                  55                  60

TTC CAG TGC CAA GTT TGC TGT TTT GTG GTT CAT AAG AGG TGC CAT GAG     240
Phe Gln Cys Gln Val Cys Cys Phe Val Val His Lys Arg Cys His Glu
65                  70                  75                  80

TTC GTT ACG TTC TCT TGT CCG GGT GCG GAT AAG GGA CCT GAC ACT GAC     288
Phe Val Thr Phe Ser Cys Pro Gly Ala Asp Lys Gly Pro Asp Thr Asp
                85                  90                  95

GAC CCC AGG AGC AAG CAC AAG TTC AAA ATC CAC ACA TAC GGA AGC CCT     336
Asp Pro Arg Ser Lys His Lys Phe Lys Ile His Thr Tyr Gly Ser Pro
            100                 105                 110

ACC TTC TGT GAT CAC TGT GGG TCC CTG CTC TAT GGA CTT ATC CAC CAA     384
Thr Phe Cys Asp His Cys Gly Ser Leu Leu Tyr Gly Leu Ile His Gln
        115                 120                 125

GGG ATG AAA TGT GAC ACC TGC GAC ATG AAT GTT CAC AAC CAG TGT GTG     432
Gly Met Lys Cys Asp Thr Cys Asp Met Asn Val His Asn Gln Cys Val
    130                 135                 140

ATC AAT GAC CCT AGC CTC TGC GGA ATG GAT CAC ACA GAG AAG AGG GGG     480
Ile Asn Asp Pro Ser Leu Cys Gly Met Asp His Thr Glu Lys Arg Gly
145                 150                 155                 160
```

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CGG ATT TAT CTG AAG GCT GAG GTC ACT GAT GAA AAG CTC CAC GTC ACG      528
Arg Ile Tyr Leu Lys Ala Glu Val Thr Asp Glu Lys Leu His Val Thr
                165                 170                 175

GTA CGA GAT GCA AAA AAT CTA ATC CCT ATG GAT CCA AAT GGG CTT TCG      576
Val Arg Asp Ala Lys Asn Leu Ile Pro Met Asp Pro Asn Gly Leu Ser
            180                 185                 190

GAT CCT TAT GTG AAG CTG AAA CTA ATC CCT GAC CCC AAG AAT GAG AGC      624
Asp Pro Tyr Val Lys Leu Lys Leu Ile Pro Asp Pro Lys Asn Glu Ser
        195                 200                 205

AAA CAG AAA ACC AAA ACC ATC CGC TCC AAC CTG AAT CCT CAG TGG AAT      672
Lys Gln Lys Thr Lys Thr Ile Arg Ser Asn Leu Asn Pro Gln Trp Asn
    210                 215                 220

GAG TCC TTC ACG TTC AAA TTA AAA CCT TCA GAC AAA GAC CGG CGA CTG      720
Glu Ser Phe Thr Phe Lys Leu Lys Pro Ser Asp Lys Asp Arg Arg Leu
225                 230                 235                 240

TCT GTA GAA ATC TGG GAC TGG GAT CGG ACG ACT CGG AAT GAC TTC ATG      768
Ser Val Glu Ile Trp Asp Trp Asp Arg Thr Thr Arg Asn Asp Phe Met
                245                 250                 255

GGA TCC CTT TCC TTT GGT GTC TCA GAG CTA ATG AAG ATG CCG GCC AGT      816
Gly Ser Leu Ser Phe Gly Val Ser Glu Leu Met Lys Met Pro Ala Ser
            260                 265                 270

GGA TGG TAT AAA GCT CAC AAC CAA GAA GAG GGC GAA TAT TAC AAC GTG      864
Gly Trp Tyr Lys Ala His Asn Gln Glu Glu Gly Glu Tyr Tyr Asn Val
        275                 280                 285

CCC ATT CCA GAA GGA GAT GAA GAA GGC AAC ATG GAA CTC AGG CAG AAG      912
Pro Ile Pro Glu Gly Asp Glu Glu Gly Asn Met Glu Leu Arg Gln Lys
    290                 295                 300

TTT GAG AAA GCC AAG CTA GGT CCT GTT GGT AAC AAA GTC ATC AGC CCT      960
Phe Glu Lys Ala Lys Leu Gly Pro Val Gly Asn Lys Val Ile Ser Pro
305                 310                 315                 320

TCA GAA GAC AGA AAG CAA CCA TCC AAC AAC CTG GAC AGA GTG AAA CTC     1008
Ser Glu Asp Arg Lys Gln Pro Ser Asn Asn Leu Asp Arg Val Lys Leu
                325                 330                 335

ACA GAC TTC AAC TTC CTC ATG GTG CTG GGG AAG GGG AGT TTT GGG AAG     1056
Thr Asp Phe Asn Phe Leu Met Val Leu Gly Lys Gly Ser Phe Gly Lys
            340                 345                 350

GTG ATG CTT GCT GAC AGG AAG GGA ACG GAG GAA CTG TAC GCC ATC AAG     1104
Val Met Leu Ala Asp Arg Lys Gly Thr Glu Glu Leu Tyr Ala Ile Lys
        355                 360                 365

ATC CTG AAG AAG GAC GTG GTG ATC CAG GAC GAC GAC GTG GAG TGC ACC     1152
Ile Leu Lys Lys Asp Val Val Ile Gln Asp Asp Asp Val Glu Cys Thr
    370                 375                 380
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ATG GTG GAG AAG CGC GTG CTG GCC CTG CTG GAC AAG CCG CCA TTT CTG 1200
Met Val Glu Lys Arg Val Leu Ala Leu Leu Asp Lys Pro Pro Phe Leu
385 390 395 400

ACA CAG CTG CAC TCC TGC TTC CAG ACA GTG GAC CGG CTG TAC TTC GTC 1248
Thr Gln Leu His Ser Cys Phe Gln Thr Val Asp Arg Leu Tyr Phe Val
405 410 415

ATG GAA TAC GTC AAC GGC GGG GAT CTT ATG TAC CAC ATT CAG CAA GTC 1296
Met Glu Tyr Val Asn Gly Gly Asp Leu Met Tyr His Ile Gln Gln Val
420 425 430

GGG AAA TTT AAG GAG CCA CAA GCA GTA TTC TAC GCA GCC GAG ATC TCC 1344
Gly Lys Phe Lys Glu Pro Gln Ala Val Phe Tyr Ala Ala Glu Ile Ser
435 440 445

ATC GGA CTG TTC TTC CTT CAT AAA AGA GGG ATC ATT TAC AGG GAT CTG 1392
Ile Gly Leu Phe Phe Leu His Lys Arg Gly Ile Ile Tyr Arg Asp Leu
450 455 460

AAG CTG AAC AAT GTC ATG CTG AAC TCA GAA GGG CAC ATC AAA ATC GCC 1440
Lys Leu Asn Asn Val Met Leu Asn Ser Glu Gly His Ile Lys Ile Ala
465 470 475 480

GAC TTC GGG ATG TGC AAG GAA CAC ATG ATG GAT GGA GTC ACG ACC AGG 1488
Asp Phe Gly Met Cys Lys Glu His Met Met Asp Gly Val Thr Thr Arg
485 490 495

ACC TTC TGC GGA ACT CCG GAC TAC ATT GCC CCA GAG ATA ATC GCT TAC 1536
Thr Phe Cys Gly Thr Pro Asp Tyr Ile Ala Pro Glu Ile Ile Ala Tyr
500 505 510

CAG CCG TAC GGG AAG TCT GTA GAT TGG TGG GCG TAC GGT GTG CTG CTG 1584
Gln Pro Tyr Gly Lys Ser Val Asp Trp Trp Ala Tyr Gly Val Leu Leu
515 520 525

TAC GAG ATG CTA GCC GGG CAG CCT CCG TTT GAT GGT GAA GAT GAA GAT 1632
Tyr Glu Met Leu Ala Gly Gln Pro Pro Phe Asp Gly Glu Asp Glu Asp
530 535 540

GAA CTG TTT CAG TCT ATA ATG GAG CAC AAC GTG TCC TAC CCC AAA TCC 1680
Glu Leu Phe Gln Ser Ile Met Glu His Asn Val Ser Tyr Pro Lys Ser
545 550 555 560

TTG TCC AAG GAA GCC GTC TCC ATC TGC AAA GGA CTT ATG ACC AAA CAG 1728
Leu Ser Lys Glu Ala Val Ser Ile Cys Lys Gly Leu Met Thr Lys Gln
565 570 575

CCT GCC AAG CGA CTG GGC TGC GGG CCC GAG GGA GAG AGG GAT GTC AGA 1776
Pro Ala Lys Arg Leu Gly Cys Gly Pro Glu Gly Glu Arg Asp Val Arg
580 585 590

GAG CAT GCC TTC TTC AGG AGG ATC GAC TGG GAG AAA CTG GAG AAC AGG 1824
Glu His Ala Phe Phe Arg Arg Ile Asp Trp Glu Lys Leu Glu Asn Arg
595 600 605

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GAG ATC CAA CCA CCA TTC AAG CCC AAA GTG TGT GGC AAA GGA GCA GAA    1872
Glu Ile Gln Pro Pro Phe Lys Pro Lys Val Cys Gly Lys Gly Ala Glu
    610                 615                 620

AAC TTT GAC AAG TTC TTC ACG CGA GGA CAG CCT GTC TTA ACA CCA CCA    1920
Asn Phe Asp Lys Phe Phe Thr Arg Gly Gln Pro Val Leu Thr Pro Pro
625                 630                 635                 640

GAT CAG CTG GTC ATT GCT AAC ATA GAC CAA TCT GAT TTT GAA GGG TTC    1968
Asp Gln Leu Val Ile Ala Asn Ile Asp Gln Ser Asp Phe Glu Gly Phe
                645                 650                 655

TCG TAT GTC AAC CCC CAG TTT GTG CAC CCA ATC TTG CAA AGT GCA GTA    2016
Ser Tyr Val Asn Pro Gln Phe Val His Pro Ile Leu Gln Ser Ala Val
            660                 665                 670

GGG CGC GCC ATG AGT AAA GGA GAA GAA CTT TTC ACT GGA GTT GTC CCA    2064
Gly Arg Ala Met Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro
        675                 680                 685

ATT CTT GTT GAA TTA GAT GGC GAT GTT AAT GGG CAA AAA TTC TCT GTT    2112
Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly Gln Lys Phe Ser Val
    690                 695                 700

AGT GGA GAG GGT GAA GGT GAT GCA ACA TAC GGA AAA CTT ACC CTT AAA    2160
Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys
705                 710                 715                 720

TTT ATT TGC ACT ACT GGG AAG CTA CCT GTT CCA TGG CCA ACG CTT GTC    2208
Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val
                725                 730                 735

ACT ACT CTC ACT TAT GGT GTT CAA TGC TTT TCT AGA TAC CCA GAT CAT    2256
Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His
            740                 745                 750

ATG AAA CAG CAT GAC TTT TTC AAG AGT GCC ATG CCC GAA GGT TAT GTA    2304
Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val
        755                 760                 765

CAG GAA AGA ACT ATA TTT TAC AAA GAT GAC GGG AAC TAC AAG ACA CGT    2352
Gln Glu Arg Thr Ile Phe Tyr Lys Asp Asp Gly Asn Tyr Lys Thr Arg
    770                 775                 780

GCT GAA GTC AAG TTT GAA GGT GAT ACC CTT GTT AAT AGA ATC GAG TTA    2400
Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu
785                 790                 795                 800

AAA GGT ATT GAT TTT AAA GAA GAT GGA AAC ATT CTT GGA CAC AAA ATG    2448
Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Met
                805                 810                 815

GAA TAC AAT TAT AAC TCA CAT AAT GTA TAC ATC ATG GCA GAC AAA CCA    2496
Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Pro
            820                 825                 830
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AAG AAT GGC ATC AAA GTT AAC TTC AAA ATT AGA CAC AAC ATT AAA GAT     2544
Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Lys Asp
        835                 840                 845

GGA AGC GTT CAA TTA GCA GAC CAT TAT CAA CAA AAT ACT CCA ATT GGC     2592
Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly
    850                 855                 860

GAT GGC CCT GTC CTT TTA CCA GAC AAC CAT TAC CTG TCC ACG CAA TCT     2640
Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser
865                 870                 875                 880

GCC CTT TCC AAA GAT CCC AAC GAA AAG AGA GAT CAC ATG ATC CTT CTT     2688
Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Ile Leu Leu
                885                 890                 895

GAG TTT GTA ACA GCT GCT GGG ATT ACA CAT GGC ATG GAT GAA CTA TAC     2736
Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr
            900                 905                 910

AAA CCT CAG GAG TAA                                                2751
Lys Pro Gln Glu
        915
```

(2) INFORMATION FOR SEQ ID NO:73:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 916 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:

```
Met Ala Asp Val Tyr Pro Ala Asn Asp Ser Thr Ala Ser Gln Asp Val
 1               5                  10                  15
Ala Asn Arg Phe Ala Arg Lys Gly Ala Leu Arg Gln Lys Asn Val His
            20                  25                  30
Glu Val Lys Asp His Lys Phe Ile Ala Arg Phe Phe Lys Gln Pro Thr
        35                  40                  45
Phe Cys Ser His Cys Thr Asp Phe Ile Trp Gly Phe Gly Lys Gln Gly
    50                  55                  60
Phe Gln Cys Gln Val Cys Cys Phe Val Val His Lys Arg Cys His Glu
65                  70                  75                  80
Phe Val Thr Phe Ser Cys Pro Gly Ala Asp Lys Gly Pro Asp Thr Asp
                85                  90                  95
Asp Pro Arg Ser Lys His Lys Phe Lys Ile His Thr Tyr Gly Ser Pro
            100                 105                 110
Thr Phe Cys Asp His Cys Gly Ser Leu Leu Tyr Gly Leu Ile His Gln
        115                 120                 125
Gly Met Lys Cys Asp Thr Cys Asp Met Asn Val His Asn Gln Cys Val
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    130                 135                 140
Ile Asn Asp Pro Ser Leu Cys Gly Met Asp His Thr Glu Lys Arg Gly
145                 150                 155                 160
Arg Ile Tyr Leu Lys Ala Glu Val Thr Asp Glu Lys Leu His Val Thr
                165                 170                 175
Val Arg Asp Ala Lys Asn Leu Ile Pro Met Asp Pro Asn Gly Leu Ser
            180                 185                 190
Asp Pro Tyr Val Lys Leu Lys Leu Ile Pro Asp Pro Lys Asn Glu Ser
        195                 200                 205
Lys Gln Lys Thr Lys Thr Ile Arg Ser Asn Leu Asn Pro Gln Trp Asn
    210                 215                 220
Glu Ser Phe Thr Phe Lys Leu Lys Pro Ser Asp Lys Asp Arg Arg Leu
225                 230                 235                 240
Ser Val Glu Ile Trp Asp Trp Asp Arg Thr Thr Arg Asn Asp Phe Met
                245                 250                 255
Gly Ser Leu Ser Phe Gly Val Ser Glu Leu Met Lys Met Pro Ala Ser
            260                 265                 270
Gly Trp Tyr Lys Ala His Asn Gln Glu Glu Gly Glu Tyr Tyr Asn Val
        275                 280                 285
Pro Ile Pro Glu Gly Asp Glu Glu Gly Asn Met Glu Leu Arg Gln Lys
    290                 295                 300
Phe Glu Lys Ala Lys Leu Gly Pro Val Gly Asn Lys Val Ile Ser Pro
305                 310                 315                 320
Ser Glu Asp Arg Lys Gln Pro Ser Asn Asn Leu Asp Arg Val Lys Leu
                325                 330                 335
Thr Asp Phe Asn Phe Leu Met Val Leu Gly Lys Gly Ser Phe Gly Lys
            340                 345                 350
Val Met Leu Ala Asp Arg Lys Gly Thr Glu Glu Leu Tyr Ala Ile Lys
        355                 360                 365
Ile Leu Lys Lys Asp Val Val Ile Gln Asp Asp Asp Val Glu Cys Thr
    370                 375                 380
Met Val Glu Lys Arg Val Leu Ala Leu Leu Asp Lys Pro Pro Phe Leu
385                 390                 395                 400
Thr Gln Leu His Ser Cys Phe Gln Thr Val Asp Arg Leu Tyr Phe Val
                405                 410                 415
Met Glu Tyr Val Asn Gly Gly Asp Leu Met Tyr His Ile Gln Gln Val
            420                 425                 430
Gly Lys Phe Lys Glu Pro Gln Ala Val Phe Tyr Ala Ala Glu Ile Ser
        435                 440                 445
Ile Gly Leu Phe Phe Leu His Lys Arg Gly Ile Ile Tyr Arg Asp Leu
    450                 455                 460
Lys Leu Asn Asn Val Met Leu Asn Ser Glu Gly His Ile Lys Ile Ala
465                 470                 475                 480
Asp Phe Gly Met Cys Lys Glu His Met Met Asp Gly Val Thr Thr Arg
                485                 490                 495
Thr Phe Cys Gly Thr Pro Asp Tyr Ile Ala Pro Glu Ile Ile Ala Tyr
            500                 505                 510
Gln Pro Tyr Gly Lys Ser Val Asp Trp Trp Ala Tyr Gly Val Leu Leu
        515                 520                 525
Tyr Glu Met Leu Ala Gly Gln Pro Pro Phe Asp Gly Glu Asp Glu Asp
    530                 535                 540
Glu Leu Phe Gln Ser Ile Met Glu His Asn Val Ser Tyr Pro Lys Ser
545                 550                 555                 560
Leu Ser Lys Glu Ala Val Ser Ile Cys Lys Gly Leu Met Thr Lys Gln
                565                 570                 575
Pro Ala Lys Arg Leu Gly Cys Gly Pro Glu Gly Glu Arg Asp Val Arg
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580 585 590
Glu His Ala Phe Phe Arg Arg Ile Asp Trp Glu Lys Leu Glu Asn Arg
595 600 605
Glu Ile Gln Pro Pro Phe Lys Pro Lys Val Cys Gly Lys Gly Ala Glu
610 615 620
Asn Phe Asp Lys Phe Phe Thr Arg Gly Gln Pro Val Leu Thr Pro Pro
625 630 635 640
Asp Gln Leu Val Ile Ala Asn Ile Asp Gln Ser Asp Phe Glu Gly Phe
645 650 655
Ser Tyr Val Asn Pro Gln Phe Val His Pro Ile Leu Gln Ser Ala Val
660 665 670
Gly Arg Ala Met Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro
675 680 685
Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly Gln Lys Phe Ser Val
690 695 700
Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys
705 710 715 720
Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val
725 730 735
Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His
740 745 750
Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val
755 760 765
Gln Glu Arg Thr Ile Phe Tyr Lys Asp Asp Gly Asn Tyr Lys Thr Arg
770 775 780
Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu
785 790 795 800
Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Met
805 810 815
Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Pro
820 825 830
Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Lys Asp
835 840 845
Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly
850 855 860
Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser
865 870 875 880
Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Ile Leu Leu
885 890 895
Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr
900 905 910
Lys Pro Gln Glu
915

(2) INFORMATION FOR SEQ ID NO:74:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2157 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence

(B) LOCATION: 1...2154
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:74:

```
ATG TCG TCC ATC TTG CCA TTC ACG CCG CCA GTT GTG AAG AGA CTG CTG      48
Met Ser Ser Ile Leu Pro Phe Thr Pro Pro Val Val Lys Arg Leu Leu
 1               5                  10                  15

GGA TGG AAG AAG TCA GCT GGT GGG TCT GGA GGA GCA GGC GGA GGA GAG      96
Gly Trp Lys Lys Ser Ala Gly Gly Ser Gly Gly Ala Gly Gly Gly Glu
            20                  25                  30

CAG AAT GGG CAG GAA GAA AAG TGG TGT GAG AAA GCA GTG AAA AGT CTG     144
Gln Asn Gly Gln Glu Glu Lys Trp Cys Glu Lys Ala Val Lys Ser Leu
        35                  40                  45

GTG AAG AAG CTA AAG AAA ACA GGA CGA TTA GAT GAG CTT GAG AAA GCC     192
Val Lys Lys Leu Lys Lys Thr Gly Arg Leu Asp Glu Leu Glu Lys Ala
    50                  55                  60

ATC ACC ACT CAA AAC TGT AAT ACT AAA TGT GTT ACC ATA CCA AGC ACT     240
Ile Thr Thr Gln Asn Cys Asn Thr Lys Cys Val Thr Ile Pro Ser Thr
65                  70                  75                  80

TGC TCT GAA ATT TGG GGA CTG AGT ACA CCA AAT ACG ATA GAT CAG TGG     288
Cys Ser Glu Ile Trp Gly Leu Ser Thr Pro Asn Thr Ile Asp Gln Trp
                85                  90                  95

GAT ACA ACA GGC CTT TAC AGC TTC TCT GAA CAA ACC AGG TCT CTT GAT     336
Asp Thr Thr Gly Leu Tyr Ser Phe Ser Glu Gln Thr Arg Ser Leu Asp
            100                 105                 110

GGT CGT CTC CAG GTA TCC CAT CGA AAA GGA TTG CCA CAT GTT ATA TAT     384
Gly Arg Leu Gln Val Ser His Arg Lys Gly Leu Pro His Val Ile Tyr
        115                 120                 125

TGC CGA TTA TGG CGC TGG CCT GAT CTT CAC AGT CAT CAT GAA CTC AAG     432
Cys Arg Leu Trp Arg Trp Pro Asp Leu His Ser His His Glu Leu Lys
    130                 135                 140

GCA ATT GAA AAC TGC GAA TAT GCT TTT AAT CTT AAA AAG GAT GAA GTA     480
Ala Ile Glu Asn Cys Glu Tyr Ala Phe Asn Leu Lys Lys Asp Glu Val
145                 150                 155                 160

TGT GTA AAC CCT TAC CAC TAT CAG AGA GTT GAG ACA CCA GTT TTG CCT     528
Cys Val Asn Pro Tyr His Tyr Gln Arg Val Glu Thr Pro Val Leu Pro
                165                 170                 175

CCA GTA TTA GTG CCC CGA CAC ACC GAG ATC CTA ACA GAA CTT CCG CCT     576
Pro Val Leu Val Pro Arg His Thr Glu Ile Leu Thr Glu Leu Pro Pro
            180                 185                 190

CTG GAT GAC TAT ACT CAC TCC ATT CCA GAA AAC ACT AAC TTC CCA GCA     624
Leu Asp Asp Tyr Thr His Ser Ile Pro Glu Asn Thr Asn Phe Pro Ala
        195                 200                 205
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GGA ATT GAG CCA CAG AGT AAT TAT ATT CCA GAA ACG CCA CCT CCT GGA      672
Gly Ile Glu Pro Gln Ser Asn Tyr Ile Pro Glu Thr Pro Pro Pro Gly
    210                 215                 220

TAT ATC AGT GAA GAT GGA GAA ACA AGT GAC CAA CAG TTG AAT CAA AGT      720
Tyr Ile Ser Glu Asp Gly Glu Thr Ser Asp Gln Gln Leu Asn Gln Ser
225                 230                 235                 240

ATG GAC ACA GGC TCT CCA GCA GAA CTA TCT CCT ACT ACT CTT TCC CCT      768
Met Asp Thr Gly Ser Pro Ala Glu Leu Ser Pro Thr Thr Leu Ser Pro
                245                 250                 255

GTT AAT CAT AGC TTG GAT TTA CAG CCA GTT ACT TAC TCA GAA CCT GCA      816
Val Asn His Ser Leu Asp Leu Gln Pro Val Thr Tyr Ser Glu Pro Ala
            260                 265                 270

TTT TGG TGT TCA ATA GCA TAT TAT GAA TTA AAT CAG AGG GTT GGA GAA      864
Phe Trp Cys Ser Ile Ala Tyr Tyr Glu Leu Asn Gln Arg Val Gly Glu
        275                 280                 285

ACC TTC CAT GCA TCA CAG CCC TCA CTC ACT GTA GAT GGC TTT ACA GAC      912
Thr Phe His Ala Ser Gln Pro Ser Leu Thr Val Asp Gly Phe Thr Asp
    290                 295                 300

CCA TCA AAT TCA GAG AGG TTC TGC TTA GGT TTA CTC TCC AAT GTT AAC      960
Pro Ser Asn Ser Glu Arg Phe Cys Leu Gly Leu Leu Ser Asn Val Asn
305                 310                 315                 320

CGA AAT GCC ACG GTA GAA ATG ACA AGA AGG CAT ATA GGA AGA GGA GTG     1008
Arg Asn Ala Thr Val Glu Met Thr Arg Arg His Ile Gly Arg Gly Val
                325                 330                 335

CGC TTA TAC TAC ATA GGT GGG GAA GTT TTT GCT GAG TGC CTA AGT GAT     1056
Arg Leu Tyr Tyr Ile Gly Gly Glu Val Phe Ala Glu Cys Leu Ser Asp
            340                 345                 350

AGT GCA ATC TTT GTG CAG AGC CCC AAT TGT AAT CAG AGA TAT GGC TGG     1104
Ser Ala Ile Phe Val Gln Ser Pro Asn Cys Asn Gln Arg Tyr Gly Trp
        355                 360                 365

CAC CCT GCA ACA GTG TGT AAA ATT CCA CCA GGC TGT AAT CTG AAG ATC     1152
His Pro Ala Thr Val Cys Lys Ile Pro Pro Gly Cys Asn Leu Lys Ile
    370                 375                 380

TTC AAC AAC CAG GAA TTT GCT GCT CTT CTG GCT CAG TCT GTT AAT CAG     1200
Phe Asn Asn Gln Glu Phe Ala Ala Leu Leu Ala Gln Ser Val Asn Gln
385                 390                 395                 400

GGT TTT GAA GCC GTC TAT CAG CTA ACT AGA ATG TGC ACC ATA AGA ATG     1248
Gly Phe Glu Ala Val Tyr Gln Leu Thr Arg Met Cys Thr Ile Arg Met
                405                 410                 415

AGT TTT GTG AAA GGG TGG GGA GCA GAA TAC CGA AGG CAG ACG GTA ACA     1296
Ser Phe Val Lys Gly Trp Gly Ala Glu Tyr Arg Arg Gln Thr Val Thr
            420                 425                 430
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AGT ACT CCT TGC TGG ATT GAA CTT CAT CTG AAT GGA CCT CTA CAG TGG   1344
Ser Thr Pro Cys Trp Ile Glu Leu His Leu Asn Gly Pro Leu Gln Trp
        435                 440                 445

TTG GAC AAA GTA TTA ACT CAG ATG GGA TCC CCT TCA GTG CGT TGC TCA   1392
Leu Asp Lys Val Leu Thr Gln Met Gly Ser Pro Ser Val Arg Cys Ser
    450                 455                 460

AGC ATG TCA TGG GTA CCG CGG GCC CGG GAT CCA CCG GTC GCC ACC ATG   1440
Ser Met Ser Trp Val Pro Arg Ala Arg Asp Pro Pro Val Ala Thr Met
465                 470                 475                 480

GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG GTC   1488
Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val
                485                 490                 495

GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC GAG   1536
Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu
            500                 505                 510

GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC TGC   1584
Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys
        515                 520                 525

ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC CTG   1632
Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu
    530                 535                 540

ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG CAG   1680
Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln
545                 550                 555                 560

CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG CGC   1728
His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg
                565                 570                 575

ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG GTG   1776
Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val
            580                 585                 590

AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC ATC   1824
Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile
        595                 600                 605

GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC AAC   1872
Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn
    610                 615                 620

TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC GGC   1920
Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly
625                 630                 635                 640

ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC GTG   1968
Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val
                645                 650                 655
```

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CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC CCC     2016
Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro
            660                 665                 670

GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG AGC     2064
Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser
        675                 680                 685

AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC GTG     2112
Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val
    690                 695                 700

ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TAA         2157
Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
705                 710                 715
```

(2) INFORMATION FOR SEQ ID NO:75:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 718 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:75:

```
Met Ser Ser Ile Leu Pro Phe Thr Pro Pro Val Val Lys Arg Leu Leu
 1               5                  10                  15
Gly Trp Lys Lys Ser Ala Gly Gly Ser Gly Gly Ala Gly Gly Gly Glu
            20                  25                  30
Gln Asn Gly Gln Glu Glu Lys Trp Cys Glu Lys Ala Val Lys Ser Leu
        35                  40                  45
Val Lys Lys Leu Lys Lys Thr Gly Arg Leu Asp Glu Leu Glu Lys Ala
    50                  55                  60
Ile Thr Thr Gln Asn Cys Asn Thr Lys Cys Val Thr Ile Pro Ser Thr
65                  70                  75                  80
Cys Ser Glu Ile Trp Gly Leu Ser Thr Pro Asn Thr Ile Asp Gln Trp
                85                  90                  95
Asp Thr Thr Gly Leu Tyr Ser Phe Ser Glu Gln Thr Arg Ser Leu Asp
            100                 105                 110
Gly Arg Leu Gln Val Ser His Arg Lys Gly Leu Pro His Val Ile Tyr
        115                 120                 125
Cys Arg Leu Trp Arg Trp Pro Asp Leu His Ser His His Glu Leu Lys
    130                 135                 140
Ala Ile Glu Asn Cys Glu Tyr Ala Phe Asn Leu Lys Lys Asp Glu Val
145                 150                 155                 160
Cys Val Asn Pro Tyr His Tyr Gln Arg Val Glu Thr Pro Val Leu Pro
                165                 170                 175
Pro Val Leu Val Pro Arg His Thr Glu Ile Leu Thr Glu Leu Pro Pro
            180                 185                 190
Leu Asp Asp Tyr Thr His Ser Ile Pro Glu Asn Thr Asn Phe Pro Ala
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          195                 200                 205
Gly Ile Glu Pro Gln Ser Asn Tyr Ile Pro Glu Thr Pro Pro Pro Gly
      210                 215                 220
Tyr Ile Ser Glu Asp Gly Glu Thr Ser Asp Gln Gln Leu Asn Gln Ser
225                 230                 235                 240
Met Asp Thr Gly Ser Pro Ala Glu Leu Ser Pro Thr Thr Leu Ser Pro
                245                 250                 255
Val Asn His Ser Leu Asp Leu Gln Pro Val Thr Tyr Ser Glu Pro Ala
            260                 265                 270
Phe Trp Cys Ser Ile Ala Tyr Tyr Glu Leu Asn Gln Arg Val Gly Glu
        275                 280                 285
Thr Phe His Ala Ser Gln Pro Ser Leu Thr Val Asp Gly Phe Thr Asp
    290                 295                 300
Pro Ser Asn Ser Glu Arg Phe Cys Leu Gly Leu Leu Ser Asn Val Asn
305                 310                 315                 320
Arg Asn Ala Thr Val Glu Met Thr Arg Arg His Ile Gly Arg Gly Val
                325                 330                 335
Arg Leu Tyr Tyr Ile Gly Gly Glu Val Phe Ala Glu Cys Leu Ser Asp
            340                 345                 350
Ser Ala Ile Phe Val Gln Ser Pro Asn Cys Asn Gln Arg Tyr Gly Trp
        355                 360                 365
His Pro Ala Thr Val Cys Lys Ile Pro Pro Gly Cys Asn Leu Lys Ile
    370                 375                 380
Phe Asn Asn Gln Glu Phe Ala Ala Leu Leu Ala Gln Ser Val Asn Gln
385                 390                 395                 400
Gly Phe Glu Ala Val Tyr Gln Leu Thr Arg Met Cys Thr Ile Arg Met
                405                 410                 415
Ser Phe Val Lys Gly Trp Gly Ala Glu Tyr Arg Arg Gln Thr Val Thr
            420                 425                 430
Ser Thr Pro Cys Trp Ile Glu Leu His Leu Asn Gly Pro Leu Gln Trp
        435                 440                 445
Leu Asp Lys Val Leu Thr Gln Met Gly Ser Pro Ser Val Arg Cys Ser
    450                 455                 460
Ser Met Ser Trp Val Pro Arg Ala Arg Asp Pro Pro Val Ala Thr Met
465                 470                 475                 480
Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val
                485                 490                 495
Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu
            500                 505                 510
Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys
        515                 520                 525
Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu
    530                 535                 540
Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln
545                 550                 555                 560
His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg
                565                 570                 575
Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val
            580                 585                 590
Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile
        595                 600                 605
Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn
    610                 615                 620
Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly
625                 630                 635                 640
Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val
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                645                 650                 655
Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro
            660                 665                 670
Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser
        675                 680                 685
Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val
    690                 695                 700
Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
705                 710                 715
```

(2) INFORMATION FOR SEQ ID NO:76:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2397 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...2394
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:76:

```
ATG GAC AAT ATG TCT ATT ACG AAT ACA CCA ACA AGT AAT GAT GCC TGT      48
Met Asp Asn Met Ser Ile Thr Asn Thr Pro Thr Ser Asn Asp Ala Cys
 1               5                  10                  15

CTG AGC ATT GTG CAT AGT TTG ATG TGC CAT AGA CAA GGT GGA GAG AGT      96
Leu Ser Ile Val His Ser Leu Met Cys His Arg Gln Gly Gly Glu Ser
            20                  25                  30

GAA ACA TTT GCA AAA AGA GCA ATT GAA AGT TTG GTA AAG AAG CTG AAG     144
Glu Thr Phe Ala Lys Arg Ala Ile Glu Ser Leu Val Lys Lys Leu Lys
        35                  40                  45

GAG AAA AAA GAT GAA TTG GAT TCT TTA ATA ACA GCT ATA ACT ACA AAT     192
Glu Lys Lys Asp Glu Leu Asp Ser Leu Ile Thr Ala Ile Thr Thr Asn
    50                  55                  60

GGA GCT CAT CCT AGT AAA TGT GTT ACC ATA CAG AGA ACA TTG GAT GGG     240
Gly Ala His Pro Ser Lys Cys Val Thr Ile Gln Arg Thr Leu Asp Gly
65                  70                  75                  80

AGG CTT CAG GTG GCT GGT CGG AAA GGA TTT CCT CAT GTG ATC TAT GCC     288
Arg Leu Gln Val Ala Gly Arg Lys Gly Phe Pro His Val Ile Tyr Ala
                85                  90                  95

CGT CTC TGG AGG TGG CCT GAT CTT CAC AAA AAT GAA CTA AAA CAT GTT     336
Arg Leu Trp Arg Trp Pro Asp Leu His Lys Asn Glu Leu Lys His Val
            100                 105                 110

AAA TAT TGT CAG TAT GCG TTT GAC TTA AAA TGT GAT AGT GTC TGT GTG     384
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Lys Tyr Cys Gln Tyr Ala Phe Asp Leu Lys Cys Asp Ser Val Cys Val
        115                 120                 125

AAT CCA TAT CAC TAC GAA CGA GTT GTA TCA CCT GGA ATT GAT CTC TCA      432
Asn Pro Tyr His Tyr Glu Arg Val Val Ser Pro Gly Ile Asp Leu Ser
    130                 135                 140

GGA TTA ACA CTG CAG AGT AAT GCT CCA TCA AGT ATG ATG GTG AAG GAT      480
Gly Leu Thr Leu Gln Ser Asn Ala Pro Ser Ser Met Met Val Lys Asp
145                 150                 155                 160

GAA TAT GTG CAT GAC TTT GAG GGA CAG CCA TCG TTG TCC ACT GAA GGA      528
Glu Tyr Val His Asp Phe Glu Gly Gln Pro Ser Leu Ser Thr Glu Gly
                165                 170                 175

CAT TCA ATT CAA ACC ATC CAG CAT CCA CCA AGT AAT CGT GCA TCG ACA      576
His Ser Ile Gln Thr Ile Gln His Pro Pro Ser Asn Arg Ala Ser Thr
            180                 185                 190

GAG ACA TAC AGC ACC CCA GCT CTG TTA GCC CCA TCT GAG TCT AAT GCT      624
Glu Thr Tyr Ser Thr Pro Ala Leu Leu Ala Pro Ser Glu Ser Asn Ala
        195                 200                 205

ACC AGC ACT GCC AAC TTT CCC AAC ATT CCT GTG GCT TCC ACA AGT CAG      672
Thr Ser Thr Ala Asn Phe Pro Asn Ile Pro Val Ala Ser Thr Ser Gln
    210                 215                 220

CCT GCC AGT ATA CTG GGG GGC AGC CAT AGT GAA GGA CTG TTG CAG ATA      720
Pro Ala Ser Ile Leu Gly Gly Ser His Ser Glu Gly Leu Leu Gln Ile
225                 230                 235                 240

GCA TCA GGG CCT CAG CCA GGA CAG CAG CAG AAT GGA TTT ACT GGT CAG      768
Ala Ser Gly Pro Gln Pro Gly Gln Gln Gln Asn Gly Phe Thr Gly Gln
                245                 250                 255

CCA GCT ACT TAC CAT CAT AAC AGC ACT ACC ACC TGG ACT GGA AGT AGG      816
Pro Ala Thr Tyr His His Asn Ser Thr Thr Thr Trp Thr Gly Ser Arg
            260                 265                 270

ACT GCA CCA TAC ACA CCT AAT TTG CCT CAC CAC CAA AAC GGC CAT CTT      864
Thr Ala Pro Tyr Thr Pro Asn Leu Pro His His Gln Asn Gly His Leu
        275                 280                 285

CAG CAC CAC CCG CCT ATG CCG CCC CAT CCC GGA CAT TAC TGG CCT GTT      912
Gln His His Pro Pro Met Pro Pro His Pro Gly His Tyr Trp Pro Val
    290                 295                 300

CAC AAT GAG CTT GCA TTC CAG CCT CCC ATT TCC AAT CAT CCT GCT CCT      960
His Asn Glu Leu Ala Phe Gln Pro Pro Ile Ser Asn His Pro Ala Pro
305                 310                 315                 320

GAG TAT TGG TGT TCC ATT GCT TAC TTT GAA ATG GAT GTT CAG GTA GGA     1008
Glu Tyr Trp Cys Ser Ile Ala Tyr Phe Glu Met Asp Val Gln Val Gly
                325                 330                 335

GAG ACA TTT AAG GTT CCT TCA AGC TGC CCT ATT GTT ACT GTT GAT GGA     1056
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Glu Thr Phe Lys Val Pro Ser Ser Cys Pro Ile Val Thr Val Asp Gly
            340                 345                 350

TAC GTG GAC CCT TCT GGA GGA GAT CGC TTT TGT TTG GGT CAA CTC TCC    1104
Tyr Val Asp Pro Ser Gly Gly Asp Arg Phe Cys Leu Gly Gln Leu Ser
        355                 360                 365

AAT GTC CAC AGG ACA GAA GCC ATT GAG AGA GCA AGG TTG CAC ATA GGC    1152
Asn Val His Arg Thr Glu Ala Ile Glu Arg Ala Arg Leu His Ile Gly
    370                 375                 380

AAA GGT GTG CAG TTG GAA TGT AAA GGT GAA GGT GAT GTT TGG GTC AGG    1200
Lys Gly Val Gln Leu Glu Cys Lys Gly Glu Gly Asp Val Trp Val Arg
385                 390                 395                 400

TGC CTT AGT GAC CAC GCG GTC TTT GTA CAG AGT TAC TAC TTA GAC AGA    1248
Cys Leu Ser Asp His Ala Val Phe Val Gln Ser Tyr Tyr Leu Asp Arg
                405                 410                 415

GAA GCT GGG CGT GCA CCT GGA GAT GCT GTT CAT AAG ATC TAC CCA AGT    1296
Glu Ala Gly Arg Ala Pro Gly Asp Ala Val His Lys Ile Tyr Pro Ser
            420                 425                 430

GCA TAT ATA AAG GTC TTT GAT TTG CGT CAG TGT CAT CGA CAG ATG CAG    1344
Ala Tyr Ile Lys Val Phe Asp Leu Arg Gln Cys His Arg Gln Met Gln
        435                 440                 445

CAG CAG GCG GCT ACT GCA CAA GCT GCA GCA GCT GCC CAG GCA GCA GCC    1392
Gln Gln Ala Ala Thr Ala Gln Ala Ala Ala Ala Ala Gln Ala Ala Ala
    450                 455                 460

GTG GCA GGA AAC ATC CCT GGC CCA GGA TCA GTA GGT GGA ATA GCT CCA    1440
Val Ala Gly Asn Ile Pro Gly Pro Gly Ser Val Gly Gly Ile Ala Pro
465                 470                 475                 480

GCT ATC AGT CTG TCA GCT GCT GCT GGA ATT GGT GTT GAT GAC CTT CGT    1488
Ala Ile Ser Leu Ser Ala Ala Ala Gly Ile Gly Val Asp Asp Leu Arg
                485                 490                 495

CGC TTA TGC ATA CTC AGG ATG AGT TTT GTG AAA GGC TGG GGA CCG GAT    1536
Arg Leu Cys Ile Leu Arg Met Ser Phe Val Lys Gly Trp Gly Pro Asp
            500                 505                 510

TAC CCA AGA CAG AGC ATC AAA GAA ACA CCT TGC TGG ATT GAA ATT CAC    1584
Tyr Pro Arg Gln Ser Ile Lys Glu Thr Pro Cys Trp Ile Glu Ile His
        515                 520                 525

TTA CAC CGG GCC CTC CAG CTC CTA GAC GAA GTA CTT CAT ACC ATG CCG    1632
Leu His Arg Ala Leu Gln Leu Leu Asp Glu Val Leu His Thr Met Pro
    530                 535                 540

ATT GCA GAC CCA CAA CCT TTA GAC TGG GAT CCA CCG GTC GCC ACC ATG    1680
Ile Ala Asp Pro Gln Pro Leu Asp Trp Asp Pro Pro Val Ala Thr Met
545                 550                 555                 560

GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG GTC    1728
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Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val
                565                 570                 575

GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC GAG    1776
Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu
            580                 585                 590

GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC TGC    1824
Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys
        595                 600                 605

ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC CTG    1872
Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu
    610                 615                 620

ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG CAG    1920
Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln
625                 630                 635                 640

CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG CGC    1968
His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg
                645                 650                 655

ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG GTG    2016
Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val
            660                 665                 670

AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC ATC    2064
Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile
        675                 680                 685

GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC AAC    2112
Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn
    690                 695                 700

TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC GGC    2160
Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly
705                 710                 715                 720

ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC GTG    2208
Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val
                725                 730                 735

CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC CCC    2256
Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro
            740                 745                 750

GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG AGC    2304
Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser
        755                 760                 765

AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC GTG    2352
Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val
    770                 775                 780

ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TAA        2397
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BNSDOCID: <WO___9845704A2_I_>

Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
785 790 795

(2) INFORMATION FOR SEQ ID NO:77:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 798 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:77:

Met Asp Asn Met Ser Ile Thr Asn Thr Pro Thr Ser Asn Asp Ala Cys
1 5 10 15
Leu Ser Ile Val His Ser Leu Met Cys His Arg Gln Gly Gly Glu Ser
20 25 30
Glu Thr Phe Ala Lys Arg Ala Ile Glu Ser Leu Val Lys Lys Leu Lys
35 40 45
Glu Lys Lys Asp Glu Leu Asp Ser Leu Ile Thr Ala Ile Thr Thr Asn
50 55 60
Gly Ala His Pro Ser Lys Cys Val Thr Ile Gln Arg Thr Leu Asp Gly
65 70 75 80
Arg Leu Gln Val Ala Gly Arg Lys Gly Phe Pro His Val Ile Tyr Ala
85 90 95
Arg Leu Trp Arg Trp Pro Asp Leu His Lys Asn Glu Leu Lys His Val
100 105 110
Lys Tyr Cys Gln Tyr Ala Phe Asp Leu Lys Cys Asp Ser Val Cys Val
115 120 125
Asn Pro Tyr His Tyr Glu Arg Val Val Ser Pro Gly Ile Asp Leu Ser
130 135 140
Gly Leu Thr Leu Gln Ser Asn Ala Pro Ser Ser Met Met Val Lys Asp
145 150 155 160
Glu Tyr Val His Asp Phe Glu Gly Gln Pro Ser Leu Ser Thr Glu Gly
165 170 175
His Ser Ile Gln Thr Ile Gln His Pro Pro Ser Asn Arg Ala Ser Thr
180 185 190
Glu Thr Tyr Ser Thr Pro Ala Leu Leu Ala Pro Ser Glu Ser Asn Ala
195 200 205
Thr Ser Thr Ala Asn Phe Pro Asn Ile Pro Val Ala Ser Thr Ser Gln
210 215 220
Pro Ala Ser Ile Leu Gly Gly Ser His Ser Glu Gly Leu Leu Gln Ile
225 230 235 240
Ala Ser Gly Pro Gln Pro Gly Gln Gln Gln Asn Gly Phe Thr Gly Gln
245 250 255
Pro Ala Thr Tyr His His Asn Ser Thr Thr Thr Trp Thr Gly Ser Arg
260 265 270
Thr Ala Pro Tyr Thr Pro Asn Leu Pro His His Gln Asn Gly His Leu
275 280 285
Gln His His Pro Pro Met Pro Pro His Pro Gly His Tyr Trp Pro Val
290 295 300
His Asn Glu Leu Ala Phe Gln Pro Pro Ile Ser Asn His Pro Ala Pro

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305                 310                 315                 320
Glu Tyr Trp Cys Ser Ile Ala Tyr Phe Glu Met Asp Val Gln Val Gly
                325                 330                 335
Glu Thr Phe Lys Val Pro Ser Ser Cys Pro Ile Val Thr Val Asp Gly
            340                 345                 350
Tyr Val Asp Pro Ser Gly Gly Asp Arg Phe Cys Leu Gly Gln Leu Ser
        355                 360                 365
Asn Val His Arg Thr Glu Ala Ile Glu Arg Ala Arg Leu His Ile Gly
    370                 375                 380
Lys Gly Val Gln Leu Glu Cys Lys Gly Glu Gly Asp Val Trp Val Arg
385                 390                 395                 400
Cys Leu Ser Asp His Ala Val Phe Val Gln Ser Tyr Tyr Leu Asp Arg
                405                 410                 415
Glu Ala Gly Arg Ala Pro Gly Asp Ala Val His Lys Ile Tyr Pro Ser
            420                 425                 430
Ala Tyr Ile Lys Val Phe Asp Leu Arg Gln Cys His Arg Gln Met Gln
        435                 440                 445
Gln Gln Ala Ala Thr Ala Gln Ala Ala Ala Ala Ala Gln Ala Ala Ala
    450                 455                 460
Val Ala Gly Asn Ile Pro Gly Pro Gly Ser Val Gly Gly Ile Ala Pro
465                 470                 475                 480
Ala Ile Ser Leu Ser Ala Ala Ala Gly Ile Gly Val Asp Asp Leu Arg
                485                 490                 495
Arg Leu Cys Ile Leu Arg Met Ser Phe Val Lys Gly Trp Gly Pro Asp
            500                 505                 510
Tyr Pro Arg Gln Ser Ile Lys Glu Thr Pro Cys Trp Ile Glu Ile His
        515                 520                 525
Leu His Arg Ala Leu Gln Leu Leu Asp Glu Val Leu His Thr Met Pro
    530                 535                 540
Ile Ala Asp Pro Gln Pro Leu Asp Trp Asp Pro Pro Val Ala Thr Met
545                 550                 555                 560
Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val
                565                 570                 575
Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu
            580                 585                 590
Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys
        595                 600                 605
Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu
    610                 615                 620
Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln
625                 630                 635                 640
His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg
                645                 650                 655
Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val
            660                 665                 670
Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile
        675                 680                 685
Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn
    690                 695                 700
Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly
705                 710                 715                 720
Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val
                725                 730                 735
Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro
            740                 745                 750
Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser
```

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          755                 760                 765
Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val
      770                 775                 780
Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
785                 790                 795
```

(2) INFORMATION FOR SEQ ID NO:78:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3138 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...3135
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:78:

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ATG GCG GGC TGG ATC CAG GCC CAG CAG CTG CAG GGA GAC GCG CTG CGC      48
Met Ala Gly Trp Ile Gln Ala Gln Gln Leu Gln Gly Asp Ala Leu Arg
 1               5                  10                  15

CAG ATG CAG GTG CTG TAC GGC CAG CAC TTC CCC ATC GAG GTC CGG CAC      96
Gln Met Gln Val Leu Tyr Gly Gln His Phe Pro Ile Glu Val Arg His
            20                  25                  30

TAC TTG GCC CAG TGG ATT GAG AGC CAG CCA TGG GAT GCC ATT GAC TTG     144
Tyr Leu Ala Gln Trp Ile Glu Ser Gln Pro Trp Asp Ala Ile Asp Leu
        35                  40                  45

GAC AAT CCC CAG GAC AGA GCC CAA GCC ACC CAG CTC CTG GAG GGC CTG     192
Asp Asn Pro Gln Asp Arg Ala Gln Ala Thr Gln Leu Leu Glu Gly Leu
    50                  55                  60

GTG CAG GAG CTG CAG AAG AAG GCG GAG CAC CAG GTG GGG GAA GAT GGG     240
Val Gln Glu Leu Gln Lys Lys Ala Glu His Gln Val Gly Glu Asp Gly
65                  70                  75                  80

TTT TTA CTG AAG ATC AAG CTG GGG CAC TAC GCC ACG CAG CTC CAG AAA     288
Phe Leu Leu Lys Ile Lys Leu Gly His Tyr Ala Thr Gln Leu Gln Lys
                85                  90                  95

ACA TAT GAC CGC TGC CCC CTG GAG CTG GTC CGC TGC ATC CGG CAC ATT     336
Thr Tyr Asp Arg Cys Pro Leu Glu Leu Val Arg Cys Ile Arg His Ile
            100                 105                 110

CTG TAC AAT GAA CAG AGG CTG GTC CGA GAA GCC AAC AAT TGC AGC TCT     384
Leu Tyr Asn Glu Gln Arg Leu Val Arg Glu Ala Asn Asn Cys Ser Ser
        115                 120                 125

CCG GCT GGG ATC CTG GTT GAC GCC ATG TCC CAG AAG CAC CTT CAG ATC     432
```

```
Pro Ala Gly Ile Leu Val Asp Ala Met Ser Gln Lys His Leu Gln Ile
    130                 135                 140

AAC CAG ACA TTT GAG GAG CTG CGA CTG GTC ACG CAG GAC ACA GAG AAT     480
Asn Gln Thr Phe Glu Glu Leu Arg Leu Val Thr Gln Asp Thr Glu Asn
145                 150                 155                 160

GAG CTG AAG AAA CTG CAG CAG ACT CAG GAG TAC TTC ATC ATC CAG TAC     528
Glu Leu Lys Lys Leu Gln Gln Thr Gln Glu Tyr Phe Ile Ile Gln Tyr
                165                 170                 175

CAG GAG AGC CTG AGG ATC CAA GCT CAG TTT GCC CAG CTG GCC CAG CTG     576
Gln Glu Ser Leu Arg Ile Gln Ala Gln Phe Ala Gln Leu Ala Gln Leu
            180                 185                 190

AGC CCC CAG GAG CGT CTG AGC CGG GAG ACG GCC CTC CAG CAG AAG CAG     624
Ser Pro Gln Glu Arg Leu Ser Arg Glu Thr Ala Leu Gln Gln Lys Gln
        195                 200                 205

GTG TCT CTG GAG GCC TGG TTG CAG CGT GAG GCA CAG ACA CTG CAG CAG     672
Val Ser Leu Glu Ala Trp Leu Gln Arg Glu Ala Gln Thr Leu Gln Gln
    210                 215                 220

TAC CGC GTG GAG CTG GCC GAG AAG CAC CAG AAG ACC CTG CAG CTG CTG     720
Tyr Arg Val Glu Leu Ala Glu Lys His Gln Lys Thr Leu Gln Leu Leu
225                 230                 235                 240

CGG AAG CAG CAG ACC ATC ATC CTG GAT GAC GAG CTG ATC CAG TGG AAG     768
Arg Lys Gln Gln Thr Ile Ile Leu Asp Asp Glu Leu Ile Gln Trp Lys
                245                 250                 255

CGG CGG CAG CAG CTG GCC GGG AAC GGC GGG CCC CCC GAG GGC AGC CTG     816
Arg Arg Gln Gln Leu Ala Gly Asn Gly Gly Pro Pro Glu Gly Ser Leu
            260                 265                 270

GAC GTG CTA CAG TCC TGG TGT GAG AAG TTG GCC GAG ATC ATC TGG CAG     864
Asp Val Leu Gln Ser Trp Cys Glu Lys Leu Ala Glu Ile Ile Trp Gln
        275                 280                 285

AAC CGG CAG CAG ATC CGC AGG GCT GAG CAC CTC TGC CAG CAG CTG CCC     912
Asn Arg Gln Gln Ile Arg Arg Ala Glu His Leu Cys Gln Gln Leu Pro
    290                 295                 300

ATC CCC GGC CCA GTG GAG GAG ATG CTG GCC GAG GTC AAC GCC ACC ATC     960
Ile Pro Gly Pro Val Glu Glu Met Leu Ala Glu Val Asn Ala Thr Ile
305                 310                 315                 320

ACG GAC ATT ATC TCA GCC CTG GTG ACC AGC ACA TTC ATC ATT GAG AAG    1008
Thr Asp Ile Ile Ser Ala Leu Val Thr Ser Thr Phe Ile Ile Glu Lys
                325                 330                 335

CAG CCT CCT CAG GTC CTG AAG ACC CAG ACC AAG TTT GCA GCC ACC GTA    1056
Gln Pro Pro Gln Val Leu Lys Thr Gln Thr Lys Phe Ala Ala Thr Val
            340                 345                 350

CGC CTG CTG GTG GGC GGG AAG CTG AAC GTG CAC ATG AAT CCC CCC CAG    1104
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BNSDOCID: <WO___9845704A2_I_>

Arg Leu Leu Val Gly Gly Lys Leu Asn Val His Met Asn Pro Pro Gln
355 360 365

GTG AAG GCC ACC ATC ATC AGT GAG CAG CAG GCC AAG TCT CTG CTT AAA 1152
Val Lys Ala Thr Ile Ile Ser Glu Gln Gln Ala Lys Ser Leu Leu Lys
370 375 380

AAT GAG AAC ACC CGC AAC GAG TGC AGT GGT GAG ATC CTG AAC AAC TGC 1200
Asn Glu Asn Thr Arg Asn Glu Cys Ser Gly Glu Ile Leu Asn Asn Cys
385 390 395 400

TGC GTG ATG GAG TAC CAC CAA GCC ACG GGC ACC CTC AGT GCC CAC TTC 1248
Cys Val Met Glu Tyr His Gln Ala Thr Gly Thr Leu Ser Ala His Phe
405 410 415

AGG AAC ATG TCA CTG AAG AGG ATC AAG CGT GCT GAC CGG CGG GGT GCA 1296
Arg Asn Met Ser Leu Lys Arg Ile Lys Arg Ala Asp Arg Arg Gly Ala
420 425 430

GAG TCC GTG ACA GAG GAG AAG TTC ACA GTC CTG TTT GAG TCT CAG TTC 1344
Glu Ser Val Thr Glu Glu Lys Phe Thr Val Leu Phe Glu Ser Gln Phe
435 440 445

AGT GTT GGC AGC AAT GAG CTT GTG TTC CAG GTG AAG ACT CTG TCC CTA 1392
Ser Val Gly Ser Asn Glu Leu Val Phe Gln Val Lys Thr Leu Ser Leu
450 455 460

CCT GTG GTT GTC ATC GTC CAC GGC AGC CAG GAC CAC AAT GCC ACG GCT 1440
Pro Val Val Val Ile Val His Gly Ser Gln Asp His Asn Ala Thr Ala
465 470 475 480

ACT GTG CTG TGG GAC AAT GCC TTT GCT GAG CCG GGC AGG GTG CCA TTT 1488
Thr Val Leu Trp Asp Asn Ala Phe Ala Glu Pro Gly Arg Val Pro Phe
485 490 495

GCC GTG CCT GAC AAA GTG CTG TGG CCG CAG CTG TGT GAG GCG CTC AAC 1536
Ala Val Pro Asp Lys Val Leu Trp Pro Gln Leu Cys Glu Ala Leu Asn
500 505 510

ATG AAA TTC AAG GCC GAA GTG CAG AGC AAC CGG GGC CTG ACC AAG GAG 1584
Met Lys Phe Lys Ala Glu Val Gln Ser Asn Arg Gly Leu Thr Lys Glu
515 520 525

AAC CTC GTG TTC CTG GCG CAG AAA CTG TTC AAC AAC AGC AGC AGC CAC 1632
Asn Leu Val Phe Leu Ala Gln Lys Leu Phe Asn Asn Ser Ser Ser His
530 535 540

CTG GAG GAC TAC AGT GGC CTG TCC GTG TCC TGG TCC CAG TTC AAC AGG 1680
Leu Glu Asp Tyr Ser Gly Leu Ser Val Ser Trp Ser Gln Phe Asn Arg
545 550 555 560

GAG AAC TTG CCG GGC TGG AAC TAC ACC TTC TGG CAG TGG TTT GAC GGG 1728
Glu Asn Leu Pro Gly Trp Asn Tyr Thr Phe Trp Gln Trp Phe Asp Gly
565 570 575

GTG ATG GAG GTG TTG AAG AAG CAC CAC AAG CCC CAC TGG AAT GAT GGG 1776

```
Val Met Glu Val Leu Lys Lys His His Lys Pro His Trp Asn Asp Gly
            580                 585                 590

GCC ATC CTA GGT TTT GTG AAT AAG CAA CAG GCC CAC GAC CTG CTC ATC    1824
Ala Ile Leu Gly Phe Val Asn Lys Gln Gln Ala His Asp Leu Leu Ile
        595                 600                 605

AAC AAG CCC GAC GGG ACC TTC TTG TTG CGC TTT AGT GAC TCA GAA ATC    1872
Asn Lys Pro Asp Gly Thr Phe Leu Leu Arg Phe Ser Asp Ser Glu Ile
    610                 615                 620

GGG GGC ATC ACC ATC GCC TGG AAG TTT GAC TCC CCG GAA CGC AAC CTG    1920
Gly Gly Ile Thr Ile Ala Trp Lys Phe Asp Ser Pro Glu Arg Asn Leu
625                 630                 635                 640

TGG AAC CTG AAA CCA TTC ACC ACG CGG GAT TTC TCC ATC AGG TCC CTG    1968
Trp Asn Leu Lys Pro Phe Thr Thr Arg Asp Phe Ser Ile Arg Ser Leu
                645                 650                 655

GCT GAC CGG CTG GGG GAC CTG AGC TAT CTC ATC TAT GTG TTT CCT GAC    2016
Ala Asp Arg Leu Gly Asp Leu Ser Tyr Leu Ile Tyr Val Phe Pro Asp
            660                 665                 670

CGC CCC AAG GAT GAG GTC TTC TCC AAG TAC TAC ACT CCT GTG CTG GCT    2064
Arg Pro Lys Asp Glu Val Phe Ser Lys Tyr Tyr Thr Pro Val Leu Ala
        675                 680                 685

AAA GCT GTT GAT GGA TAT GTG AAA CCA CAG ATC AAG CAA GTG GTC CCT    2112
Lys Ala Val Asp Gly Tyr Val Lys Pro Gln Ile Lys Gln Val Val Pro
    690                 695                 700

GAG TTT GTG AAT GCA TCT GCA GAT GCT GGG GGC AGC AGC GCC ACG TAC    2160
Glu Phe Val Asn Ala Ser Ala Asp Ala Gly Gly Ser Ser Ala Thr Tyr
705                 710                 715                 720

ATG GAC CAG GCC CCC TCC CCA GCT GTG TGC CCC CAG GCT CCC TAT AAC    2208
Met Asp Gln Ala Pro Ser Pro Ala Val Cys Pro Gln Ala Pro Tyr Asn
                725                 730                 735

ATG TAC CCA CAG AAC CCT GAC CAT GTA CTC GAT CAG GAT GGA GAA TTC    2256
Met Tyr Pro Gln Asn Pro Asp His Val Leu Asp Gln Asp Gly Glu Phe
            740                 745                 750

GAC CTG GAT GAG ACC ATG GAT GTG GCC AGG CAC GTG GAG GAA CTC TTA    2304
Asp Leu Asp Glu Thr Met Asp Val Ala Arg His Val Glu Glu Leu Leu
        755                 760                 765

CGC CGA CCA ATG GAC AGT CTT GAC TCC CGC CTC TCG CCC CCT GCC GGT    2352
Arg Arg Pro Met Asp Ser Leu Asp Ser Arg Leu Ser Pro Pro Ala Gly
    770                 775                 780

CTT TTC ACC TCT GCC AGA GGC TCC CTC TCA TGG GTA CCG CGG GCC CGG    2400
Leu Phe Thr Ser Ala Arg Gly Ser Leu Ser Trp Val Pro Arg Ala Arg
785                 790                 795                 800

GAT CCA CCG GTC GCC ACC ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC    2448
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Asp Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr
                805                 810                 815

GGG GTG GTG CCC ATC CTG GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC    2496
Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His
            820                 825                 830

AAG TTC AGC GTG TCC GGC GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG    2544
Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys
        835                 840                 845

CTG ACC CTG AAG TTC ATC TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG    2592
Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp
    850                 855                 860

CCC ACC CTC GTG ACC ACC CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC    2640
Pro Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg
865                 870                 875                 880

TAC CCC GAC CAC ATG AAG CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC    2688
Tyr Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro
                885                 890                 895

GAA GGC TAC GTC CAG GAG CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC    2736
Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn
            900                 905                 910

TAC AAG ACC CGC GCC GAG GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC    2784
Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn
        915                 920                 925

CGC ATC GAG CTG AAG GGC ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG    2832
Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu
    930                 935                 940

GGG CAC AAG CTG GAG TAC AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG    2880
Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met
945                 950                 955                 960

GCC GAC AAG CAG AAG AAC GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC    2928
Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His
                965                 970                 975

AAC ATC GAG GAC GGC AGC GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC    2976
Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn
            980                 985                 990

ACC CCC ATC GGC GAC GGC CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG    3024
Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu
        995                1000                1005

AGC ACC CAG TCC GCC CTG AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC    3072
Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His
   1010                1015                1020

ATG GTC CTG CTG GAG TTC GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG    3120
```


BNSDOCID: <WO__9845704A2_I_>

```
Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met
1025                1030                1035                1040

GAC GAG CTG TAC AAG TAA                                        3138
Asp Glu Leu Tyr Lys
               1045
```

(2) INFORMATION FOR SEQ ID NO:79:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1045 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:79:

```
Met Ala Gly Trp Ile Gln Ala Gln Gln Leu Gln Gly Asp Ala Leu Arg
 1               5                  10                  15
Gln Met Gln Val Leu Tyr Gly Gln His Phe Pro Ile Glu Val Arg His
            20                  25                  30
Tyr Leu Ala Gln Trp Ile Glu Ser Gln Pro Trp Asp Ala Ile Asp Leu
        35                  40                  45
Asp Asn Pro Gln Asp Arg Ala Gln Ala Thr Gln Leu Leu Glu Gly Leu
    50                  55                  60
Val Gln Glu Leu Gln Lys Lys Ala Glu His Gln Val Gly Glu Asp Gly
65                  70                  75                  80
Phe Leu Leu Lys Ile Lys Leu Gly His Tyr Ala Thr Gln Leu Gln Lys
                85                  90                  95
Thr Tyr Asp Arg Cys Pro Leu Glu Leu Val Arg Cys Ile Arg His Ile
            100                 105                 110
Leu Tyr Asn Glu Gln Arg Leu Val Arg Glu Ala Asn Asn Cys Ser Ser
        115                 120                 125
Pro Ala Gly Ile Leu Val Asp Ala Met Ser Gln Lys His Leu Gln Ile
    130                 135                 140
Asn Gln Thr Phe Glu Glu Leu Arg Leu Val Thr Gln Asp Thr Glu Asn
145                 150                 155                 160
Glu Leu Lys Lys Leu Gln Gln Thr Gln Glu Tyr Phe Ile Ile Gln Tyr
                165                 170                 175
Gln Glu Ser Leu Arg Ile Gln Ala Gln Phe Ala Gln Leu Ala Gln Leu
            180                 185                 190
Ser Pro Gln Glu Arg Leu Ser Arg Glu Thr Ala Leu Gln Gln Lys Gln
        195                 200                 205
Val Ser Leu Glu Ala Trp Leu Gln Arg Glu Ala Gln Thr Leu Gln Gln
    210                 215                 220
Tyr Arg Val Glu Leu Ala Glu Lys His Gln Lys Thr Leu Gln Leu Leu
225                 230                 235                 240
Arg Lys Gln Gln Thr Ile Ile Leu Asp Asp Glu Leu Ile Gln Trp Lys
                245                 250                 255
Arg Arg Gln Gln Leu Ala Gly Asn Gly Gly Pro Pro Glu Gly Ser Leu
            260                 265                 270
Asp Val Leu Gln Ser Trp Cys Glu Lys Leu Ala Glu Ile Ile Trp Gln
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          275                 280                 285
Asn Arg Gln Gln Ile Arg Arg Ala Glu His Leu Cys Gln Gln Leu Pro
    290                 295                 300
Ile Pro Gly Pro Val Glu Glu Met Leu Ala Glu Val Asn Ala Thr Ile
305                 310                 315                 320
Thr Asp Ile Ile Ser Ala Leu Val Thr Ser Thr Phe Ile Ile Glu Lys
                325                 330                 335
Gln Pro Pro Gln Val Leu Lys Thr Gln Thr Lys Phe Ala Ala Thr Val
            340                 345                 350
Arg Leu Leu Val Gly Gly Lys Leu Asn Val His Met Asn Pro Pro Gln
        355                 360                 365
Val Lys Ala Thr Ile Ile Ser Glu Gln Gln Ala Lys Ser Leu Leu Lys
    370                 375                 380
Asn Glu Asn Thr Arg Asn Glu Cys Ser Gly Glu Ile Leu Asn Asn Cys
385                 390                 395                 400
Cys Val Met Glu Tyr His Gln Ala Thr Gly Thr Leu Ser Ala His Phe
                405                 410                 415
Arg Asn Met Ser Leu Lys Arg Ile Lys Arg Ala Asp Arg Arg Gly Ala
            420                 425                 430
Glu Ser Val Thr Glu Glu Lys Phe Thr Val Leu Phe Glu Ser Gln Phe
        435                 440                 445
Ser Val Gly Ser Asn Glu Leu Val Phe Gln Val Lys Thr Leu Ser Leu
    450                 455                 460
Pro Val Val Val Ile Val His Gly Ser Gln Asp His Asn Ala Thr Ala
465                 470                 475                 480
Thr Val Leu Trp Asp Asn Ala Phe Ala Glu Pro Gly Arg Val Pro Phe
                485                 490                 495
Ala Val Pro Asp Lys Val Leu Trp Pro Gln Leu Cys Glu Ala Leu Asn
            500                 505                 510
Met Lys Phe Lys Ala Glu Val Gln Ser Asn Arg Gly Leu Thr Lys Glu
        515                 520                 525
Asn Leu Val Phe Leu Ala Gln Lys Leu Phe Asn Asn Ser Ser Ser His
    530                 535                 540
Leu Glu Asp Tyr Ser Gly Leu Ser Val Ser Trp Ser Gln Phe Asn Arg
545                 550                 555                 560
Glu Asn Leu Pro Gly Trp Asn Tyr Thr Phe Trp Gln Trp Phe Asp Gly
                565                 570                 575
Val Met Glu Val Leu Lys Lys His His Lys Pro His Trp Asn Asp Gly
            580                 585                 590
Ala Ile Leu Gly Phe Val Asn Lys Gln Gln Ala His Asp Leu Leu Ile
        595                 600                 605
Asn Lys Pro Asp Gly Thr Phe Leu Leu Arg Phe Ser Asp Ser Glu Ile
    610                 615                 620
Gly Gly Ile Thr Ile Ala Trp Lys Phe Asp Ser Pro Glu Arg Asn Leu
625                 630                 635                 640
Trp Asn Leu Lys Pro Phe Thr Thr Arg Asp Phe Ser Ile Arg Ser Leu
                645                 650                 655
Ala Asp Arg Leu Gly Asp Leu Ser Tyr Leu Ile Tyr Val Phe Pro Asp
            660                 665                 670
Arg Pro Lys Asp Glu Val Phe Ser Lys Tyr Tyr Thr Pro Val Leu Ala
        675                 680                 685
Lys Ala Val Asp Gly Tyr Val Lys Pro Gln Ile Lys Gln Val Val Pro
    690                 695                 700
Glu Phe Val Asn Ala Ser Ala Asp Ala Gly Gly Ser Ser Ala Thr Tyr
705                 710                 715                 720
Met Asp Gln Ala Pro Ser Pro Ala Val Cys Pro Gln Ala Pro Tyr Asn
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725 730 735
Met Tyr Pro Gln Asn Pro Asp His Val Leu Asp Gln Asp Gly Glu Phe
740 745 750
Asp Leu Asp Glu Thr Met Asp Val Ala Arg His Val Glu Glu Leu Leu
755 760 765
Arg Arg Pro Met Asp Ser Leu Asp Ser Arg Leu Ser Pro Pro Ala Gly
770 775 780
Leu Phe Thr Ser Ala Arg Gly Ser Leu Ser Trp Val Pro Arg Ala Arg
785 790 795 800
Asp Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr
805 810 815
Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His
820 825 830
Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys
835 840 845
Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp
850 855 860
Pro Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg
865 870 875 880
Tyr Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro
885 890 895
Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn
900 905 910
Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn
915 920 925
Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu
930 935 940
Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met
945 950 955 960
Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His
965 970 975
Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn
980 985 990
Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu
995 1000 1005
Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His
1010 1015 1020
Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met
025 1030 1035 1040
Asp Glu Leu Tyr Lys
1045

(2) INFORMATION FOR SEQ ID NO:80:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 28 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:80:

TGGGATCCTC AGGCCGTGCT GCTGGCCG 28

(2) INFORMATION FOR SEQ ID NO:81:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:81:

GTCTCGAGGG AGCATGGGCA CCTTGCG 27

(2) INFORMATION FOR SEQ ID NO:82:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:82:

TGGGATCCGA GAAGTCTATA TCCCATC 27

(2) INFORMATION FOR SEQ ID NO:83:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 28 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:83:

TGGGATCCTT AGAAGTCTAT ATCCCATC 28

(2) INFORMATION FOR SEQ ID NO:84:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 28 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:84:

GTCTCGAGCC ATGAACGCCC CCGAGCGG 28

(2) INFORMATION FOR SEQ ID NO:85:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 30 base pairs
(B) TYPE: nucleic acid

BNSDOCID: <WO___9845704A2_I_>

(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:85:

GTGAATTCTC GTCTGATTTC TGGCAGGAGG 30

(2) INFORMATION FOR SEQ ID NO:86:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 30 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:86:

GTGAATTCTT TACGTCTGAT TTCTGGCAGG 30

(2) INFORMATION FOR SEQ ID NO:87:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 34 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:87:

GTCTCGAGCC ATGGACGAAC TGTTCCCCCT CATC 34

(2) INFORMATION FOR SEQ ID NO:88:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 31 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:88:

GTGGATCCAA GGAGCTGATC TGACTCAGCA G 31

(2) INFORMATION FOR SEQ ID NO:89:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 32 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

BNSDOCID: <WO___9845704A2_I_>

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:89:

GTGGATCCTT AGGAGCTGAT CTGACTCAGC AG 32

(2) INFORMATION FOR SEQ ID NO:90:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 32 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:90:

CCTCCTAAGC TTATCATGGA CCATTATGAT TC 32

(2) INFORMATION FOR SEQ ID NO:91:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 33 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:91:

CCTCCTGGAT CCCTGCGCAG GATGATGGTC CAG 33

(2) INFORMATION FOR SEQ ID NO:92:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 45 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:92:

GGATGGAAGC TTCAATGGCT GCCATCCGGA AGAAACTGGT GATTG 45

(2) INFORMATION FOR SEQ ID NO:93:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 45 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:93:

GGATGGGGAT CCTCACAAGA CAAGGCAACC AGATTTTTTC TTCCC 45

(2) INFORMATION FOR SEQ ID NO:94:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 29 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:94:

GGGAAGCTTC CATGAGCGAG ACGGTCATC 29

(2) INFORMATION FOR SEQ ID NO:95:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 28 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:95:

CCCGGATCCT CAGGGAGAAC CCCGCTTC 28

(2) INFORMATION FOR SEQ ID NO:96:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 30 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:96:

GTGAATTCGA CCATGGAGCG GCCCCCGGGG 30

(2) INFORMATION FOR SEQ ID NO:97:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:97:

GTGGTACCCA TTCTGTTAAC CAACTCC 27

(2) INFORMATION FOR SEQ ID NO:98:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 28 base pairs

(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:98:

GTGGTACCTC ATTCTGTTAA CCAACTCC 28

(2) INFORMATION FOR SEQ ID NO:99:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 28 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:99:

GTCTCGAGAG ATGCTGTCCC GTGGGTGG 28

(2) INFORMATION FOR SEQ ID NO:100:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:100:

GTGAATTCGC TTCCTCTTGA GGGAACC 27

(2) INFORMATION FOR SEQ ID NO:101:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:101:

GTGAATTCAC TTCCTCTTGA GGGAACC 27

(2) INFORMATION FOR SEQ ID NO:102:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 29 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:102:

GTCTCGAGCC ATGGAGAACT TCCAAAAGG 29

(2) INFORMATION FOR SEQ ID NO:103:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 28 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:103:

GTGGATCCCA GAGTCGAAGA TGGGGTAC 28

(2) INFORMATION FOR SEQ ID NO:104:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 29 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:104:

GTGGATCCTC AGAGTCGAAG ATGGGGTAC 29

(2) INFORMATION FOR SEQ ID NO:105:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 30 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:105:

GTGAATTCGG CGATGCCAGA CCCCGCGGCG 30

(2) INFORMATION FOR SEQ ID NO:106:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 32 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:106:

GTGGATCCCA GGCACAGGCA GCCTCAGCCT TC 32

(2) INFORMATION FOR SEQ ID NO:107:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 33 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:107:

GTGGATCCTC AGGCACAGGC AGCCTCAGCC TTC 33

(2) INFORMATION FOR SEQ ID NO:108:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2616 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...2613
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:108:

```
ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15

GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30

GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45

TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC     192
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60

CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG     240
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80

CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG     288
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95

CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG     336
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Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110

GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC     384
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125

ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC     432
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140

AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC     480
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160

GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC     528
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175

GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC     576
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190

CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG     624
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205

AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC     672
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220

GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC     720
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240

GGA CTC AGA TCT CGA GCT CAA GCT TCG AAT TCG GCG ATG CCA GAC CCC     768
Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Ala Met Pro Asp Pro
                245                 250                 255

GCG GCG CAC CTG CCC TTC TTC TAC GGC AGC ATC TCG CGT GCC GAG GCC     816
Ala Ala His Leu Pro Phe Phe Tyr Gly Ser Ile Ser Arg Ala Glu Ala
            260                 265                 270

GAG GAG CAC CTG AAG CTG GCG GGC ATG GCG GAC GGG CTC TTC CTG CTG     864
Glu Glu His Leu Lys Leu Ala Gly Met Ala Asp Gly Leu Phe Leu Leu
        275                 280                 285

CGC CAG TGC CTG CGC TCG CTG GGC GGC TAT GTG CTG TCG CTC GTG CAC     912
Arg Gln Cys Leu Arg Ser Leu Gly Gly Tyr Val Leu Ser Leu Val His
    290                 295                 300

GAT GTG CGC TTC CAC CAC TTT CCC ATC GAG CGC CAG CTC AAC GGC ACC     960
Asp Val Arg Phe His His Phe Pro Ile Glu Arg Gln Leu Asn Gly Thr
305                 310                 315                 320

TAC GCC ATT GCC GGC GGC AAA GCG CAC TGT GGA CCG GCA GAG CTC TGC    1008
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Tyr Ala Ile Ala Gly Gly Lys Ala His Cys Gly Pro Ala Glu Leu Cys
325                 330                 335

GAG TTC TAC TCG CGC GAC CCC GAC GGG CTG CCC TGC AAC CTG CGC AAG    1056
Glu Phe Tyr Ser Arg Asp Pro Asp Gly Leu Pro Cys Asn Leu Arg Lys
            340                 345                 350

CCG TGC AAC CGG CCG TCG GGC CTC GAG CCG CAG CCG GGG GTC TTC GAC    1104
Pro Cys Asn Arg Pro Ser Gly Leu Glu Pro Gln Pro Gly Val Phe Asp
        355                 360                 365

TGC CTG CGA GAC GCC ATG GTG CGT GAC TAC GTG CGC CAG ACG TGG AAG    1152
Cys Leu Arg Asp Ala Met Val Arg Asp Tyr Val Arg Gln Thr Trp Lys
    370                 375                 380

CTG GAG GGC GAG GCC CTG GAG CAG GCC ATC ATC AGC CAG GCC CCG CAG    1200
Leu Glu Gly Glu Ala Leu Glu Gln Ala Ile Ile Ser Gln Ala Pro Gln
385                 390                 395                 400

GTG GAG AAG CTC ATT GCT ACG ACG GCC CAC GAG CGG ATG CCC TGG TAC    1248
Val Glu Lys Leu Ile Ala Thr Thr Ala His Glu Arg Met Pro Trp Tyr
                405                 410                 415

CAC AGC AGC CTG ACG CGT GAG GAG GCC GAG CGC AAA CTT TAC TCT GGG    1296
His Ser Ser Leu Thr Arg Glu Glu Ala Glu Arg Lys Leu Tyr Ser Gly
            420                 425                 430

GCG CAG ACC GAC GGC AAG TTC CTG CTG AGG CCG CGG AAG GAG CAG GGC    1344
Ala Gln Thr Asp Gly Lys Phe Leu Leu Arg Pro Arg Lys Glu Gln Gly
        435                 440                 445

ACA TAC GCC CTG TCC CTC ATC TAT GGG AAG ACG GTG TAC CAC TAC CTC    1392
Thr Tyr Ala Leu Ser Leu Ile Tyr Gly Lys Thr Val Tyr His Tyr Leu
    450                 455                 460

ATC AGC CAA GAC AAG GCG GGC AAG TAC TGC ATT CCC GAG GGC ACC AAG    1440
Ile Ser Gln Asp Lys Ala Gly Lys Tyr Cys Ile Pro Glu Gly Thr Lys
465                 470                 475                 480

TTT GAC ACG CTC TGG CAG CTG GTG GAG TAT CTG AAG CTG AAG GCG GAC    1488
Phe Asp Thr Leu Trp Gln Leu Val Glu Tyr Leu Lys Leu Lys Ala Asp
                485                 490                 495

GGG CTC ATC TAC TGC CTG AAG GAG GCC TGC CCC AAC AGC AGT GCC AGC    1536
Gly Leu Ile Tyr Cys Leu Lys Glu Ala Cys Pro Asn Ser Ser Ala Ser
            500                 505                 510

AAC GCC TCA GGG GCT GCT GCT CCC ACA CTC CCA GCC CAC CCA TCC ACG    1584
Asn Ala Ser Gly Ala Ala Ala Pro Thr Leu Pro Ala His Pro Ser Thr
        515                 520                 525

TTG ACT CAT CCT CAG AGA CGA ATC GAC ACC CTC AAC TCA GAT GGA TAC    1632
Leu Thr His Pro Gln Arg Arg Ile Asp Thr Leu Asn Ser Asp Gly Tyr
    530                 535                 540

ACC CCT GAG CCA GCA CGC ATA ACG TCC CCA GAC AAA CCG CGG CCG ATG    1680
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Thr Pro Glu Pro Ala Arg Ile Thr Ser Pro Asp Lys Pro Arg Pro Met
545                 550                 555                 560

CCC ATG GAC ACG AGC GTG TAT GAG AGC CCC TAC AGC GAC CCA GAG GAG    1728
Pro Met Asp Thr Ser Val Tyr Glu Ser Pro Tyr Ser Asp Pro Glu Glu
                565                 570                 575

CTC AAG GAC AAG AAG CTC TTC CTG AAG CGC GAT AAC CTC CTC ATA GCT    1776
Leu Lys Asp Lys Lys Leu Phe Leu Lys Arg Asp Asn Leu Leu Ile Ala
            580                 585                 590

GAC ATT GAA CTT GGC TGC GGC AAC TTT GGC TCA GTG CGC CAG GGC GTG    1824
Asp Ile Glu Leu Gly Cys Gly Asn Phe Gly Ser Val Arg Gln Gly Val
        595                 600                 605

TAC CGC ATG CGC AAG AAG CAG ATC GAC GTG GCC ATC AAG GTG CTG AAG    1872
Tyr Arg Met Arg Lys Lys Gln Ile Asp Val Ala Ile Lys Val Leu Lys
    610                 615                 620

CAG GGC ACG GAG AAG GCA GAC ACG GAA GAG ATG ATG CGC GAG GCG CAG    1920
Gln Gly Thr Glu Lys Ala Asp Thr Glu Glu Met Met Arg Glu Ala Gln
625                 630                 635                 640

ATC ATG CAC CAG CTG GAC AAC CCC TAC ATC GTG CGG CTC ATT GGC GTC    1968
Ile Met His Gln Leu Asp Asn Pro Tyr Ile Val Arg Leu Ile Gly Val
                645                 650                 655

TGC CAG GCC GAG GCC CTC ATG CTG GTC ATG GAG ATG GCT GGG GGC GGG    2016
Cys Gln Ala Glu Ala Leu Met Leu Val Met Glu Met Ala Gly Gly Gly
            660                 665                 670

CCG CTG CAC AAG TTC CTG GTC GGC AAG AGG GAG GAG ATC CCT GTG AGC    2064
Pro Leu His Lys Phe Leu Val Gly Lys Arg Glu Glu Ile Pro Val Ser
        675                 680                 685

AAT GTG GCC GAG CTG CTG CAC CAG GTG TCC ATG GGG ATG AAG TAC CTG    2112
Asn Val Ala Glu Leu Leu His Gln Val Ser Met Gly Met Lys Tyr Leu
    690                 695                 700

GAG GAG AAG AAC TTT GTG CAC CGT GAC CTG GCG GCC CGC AAC GTC CTG    2160
Glu Glu Lys Asn Phe Val His Arg Asp Leu Ala Ala Arg Asn Val Leu
705                 710                 715                 720

CTG GTT AAC CGG CAC TAC GCC AAG ATC AGC GAC TTT GGC CTC TCC AAA    2208
Leu Val Asn Arg His Tyr Ala Lys Ile Ser Asp Phe Gly Leu Ser Lys
                725                 730                 735

GCA CTG GGT GCC GAC GAC AGC TAC TAC ACT GCC CGC TCA GCA GGG AAG    2256
Ala Leu Gly Ala Asp Asp Ser Tyr Tyr Thr Ala Arg Ser Ala Gly Lys
            740                 745                 750

TGG CCG CTC AAG TGG TAC GCA CCC GAA TGC ATC AAC TTC CGC AAG TTC    2304
Trp Pro Leu Lys Trp Tyr Ala Pro Glu Cys Ile Asn Phe Arg Lys Phe
        755                 760                 765

TCC AGC CGC AGC GAT GTC TGG AGC TAT GGG GTC ACC ATG TGG GAG GCC    2352
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Ser Ser Arg Ser Asp Val Trp Ser Tyr Gly Val Thr Met Trp Glu Ala
    770                 775                 780

TTG TCC TAC GGC CAG AAG CCC TAC AAG AAG ATG AAA GGG CCG GAG GTC    2400
Leu Ser Tyr Gly Gln Lys Pro Tyr Lys Lys Met Lys Gly Pro Glu Val
785                 790                 795                 800

ATG GCC TTC ATC GAG CAG GGC AAG CGG ATG GAG TGC CCA CCA GAG TGT    2448
Met Ala Phe Ile Glu Gln Gly Lys Arg Met Glu Cys Pro Pro Glu Cys
                805                 810                 815

CCA CCC GAA CTG TAC GCA CTC ATG AGT GAC TGC TGG ATC TAC AAG TGG    2496
Pro Pro Glu Leu Tyr Ala Leu Met Ser Asp Cys Trp Ile Tyr Lys Trp
            820                 825                 830

GAG GAT CGC CCC GAC TTC CTG ACC GTG GAG CAG CGC ATG CGA GCC TGT    2544
Glu Asp Arg Pro Asp Phe Leu Thr Val Glu Gln Arg Met Arg Ala Cys
        835                 840                 845

TAC TAC AGC CTG GCC AGC AAG GTG GAA GGG CCC CCA GGC AGC ACA CAG    2592
Tyr Tyr Ser Leu Ala Ser Lys Val Glu Gly Pro Pro Gly Ser Thr Gln
    850                 855                 860

AAG GCT GAG GCT GCC TGT GCC TGA                                   2616
Lys Ala Glu Ala Ala Cys Ala
865                 870
```

(2) INFORMATION FOR SEQ ID NO:109:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 871 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:109:

```
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
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                115                 120                 125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
            130                 135                 140
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240
Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Ala Met Pro Asp Pro
                245                 250                 255
Ala Ala His Leu Pro Phe Phe Tyr Gly Ser Ile Ser Arg Ala Glu Ala
            260                 265                 270
Glu Glu His Leu Lys Leu Ala Gly Met Ala Asp Gly Leu Phe Leu Leu
        275                 280                 285
Arg Gln Cys Leu Arg Ser Leu Gly Gly Tyr Val Leu Ser Leu Val His
    290                 295                 300
Asp Val Arg Phe His His Phe Pro Ile Glu Arg Gln Leu Asn Gly Thr
305                 310                 315                 320
Tyr Ala Ile Ala Gly Gly Lys Ala His Cys Gly Pro Ala Glu Leu Cys
                325                 330                 335
Glu Phe Tyr Ser Arg Asp Pro Asp Gly Leu Pro Cys Asn Leu Arg Lys
            340                 345                 350
Pro Cys Asn Arg Pro Ser Gly Leu Glu Pro Gln Pro Gly Val Phe Asp
        355                 360                 365
Cys Leu Arg Asp Ala Met Val Arg Asp Tyr Val Arg Gln Thr Trp Lys
    370                 375                 380
Leu Glu Gly Glu Ala Leu Glu Gln Ala Ile Ile Ser Gln Ala Pro Gln
385                 390                 395                 400
Val Glu Lys Leu Ile Ala Thr Thr Ala His Glu Arg Met Pro Trp Tyr
                405                 410                 415
His Ser Ser Leu Thr Arg Glu Glu Ala Glu Arg Lys Leu Tyr Ser Gly
            420                 425                 430
Ala Gln Thr Asp Gly Lys Phe Leu Leu Arg Pro Arg Lys Glu Gln Gly
        435                 440                 445
Thr Tyr Ala Leu Ser Leu Ile Tyr Gly Lys Thr Val Tyr His Tyr Leu
    450                 455                 460
Ile Ser Gln Asp Lys Ala Gly Lys Tyr Cys Ile Pro Glu Gly Thr Lys
465                 470                 475                 480
Phe Asp Thr Leu Trp Gln Leu Val Glu Tyr Leu Lys Leu Lys Ala Asp
                485                 490                 495
Gly Leu Ile Tyr Cys Leu Lys Glu Ala Cys Pro Asn Ser Ser Ala Ser
            500                 505                 510
Asn Ala Ser Gly Ala Ala Ala Pro Thr Leu Pro Ala His Pro Ser Thr
        515                 520                 525
Leu Thr His Pro Gln Arg Arg Ile Asp Thr Leu Asn Ser Asp Gly Tyr
    530                 535                 540
Thr Pro Glu Pro Ala Arg Ile Thr Ser Pro Asp Lys Pro Arg Pro Met
545                 550                 555                 560
Pro Met Asp Thr Ser Val Tyr Glu Ser Pro Tyr Ser Asp Pro Glu Glu
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565 570 575
Leu Lys Asp Lys Lys Leu Phe Leu Lys Arg Asp Asn Leu Leu Ile Ala
580 585 590
Asp Ile Glu Leu Gly Cys Gly Asn Phe Gly Ser Val Arg Gln Gly Val
595 600 605
Tyr Arg Met Arg Lys Lys Gln Ile Asp Val Ala Ile Lys Val Leu Lys
610 615 620
Gln Gly Thr Glu Lys Ala Asp Thr Glu Glu Met Met Arg Glu Ala Gln
625 630 635 640
Ile Met His Gln Leu Asp Asn Pro Tyr Ile Val Arg Leu Ile Gly Val
645 650 655
Cys Gln Ala Glu Ala Leu Met Leu Val Met Glu Met Ala Gly Gly Gly
660 665 670
Pro Leu His Lys Phe Leu Val Gly Lys Arg Glu Glu Ile Pro Val Ser
675 680 685
Asn Val Ala Glu Leu Leu His Gln Val Ser Met Gly Met Lys Tyr Leu
690 695 700
Glu Glu Lys Asn Phe Val His Arg Asp Leu Ala Ala Arg Asn Val Leu
705 710 715 720
Leu Val Asn Arg His Tyr Ala Lys Ile Ser Asp Phe Gly Leu Ser Lys
725 730 735
Ala Leu Gly Ala Asp Asp Ser Tyr Tyr Thr Ala Arg Ser Ala Gly Lys
740 745 750
Trp Pro Leu Lys Trp Tyr Ala Pro Glu Cys Ile Asn Phe Arg Lys Phe
755 760 765
Ser Ser Arg Ser Asp Val Trp Ser Tyr Gly Val Thr Met Trp Glu Ala
770 775 780
Leu Ser Tyr Gly Gln Lys Pro Tyr Lys Lys Met Lys Gly Pro Glu Val
785 790 795 800
Met Ala Phe Ile Glu Gln Gly Lys Arg Met Glu Cys Pro Pro Glu Cys
805 810 815
Pro Pro Glu Leu Tyr Ala Leu Met Ser Asp Cys Trp Ile Tyr Lys Trp
820 825 830
Glu Asp Arg Pro Asp Phe Leu Thr Val Glu Gln Arg Met Arg Ala Cys
835 840 845
Tyr Tyr Ser Leu Ala Ser Lys Val Glu Gly Pro Pro Gly Ser Thr Gln
850 855 860
Lys Ala Glu Ala Ala Cys Ala
865 870

(2) INFORMATION FOR SEQ ID NO:110:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2598 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...2595
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:110:

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ATG CCA GAC CCC GCG GCG CAC CTG CCC TTC TTC TAC GGC AGC ATC TCG      48
Met Pro Asp Pro Ala Ala His Leu Pro Phe Phe Tyr Gly Ser Ile Ser
 1               5                  10                  15

CGT GCC GAG GCC GAG GAG CAC CTG AAG CTG GCG GGC ATG GCG GAC GGG      96
Arg Ala Glu Ala Glu Glu His Leu Lys Leu Ala Gly Met Ala Asp Gly
            20                  25                  30

CTC TTC CTG CTG CGC CAG TGC CTG CGC TCG CTG GGC GGC TAT GTG CTG     144
Leu Phe Leu Leu Arg Gln Cys Leu Arg Ser Leu Gly Gly Tyr Val Leu
        35                  40                  45

TCG CTC GTG CAC GAT GTG CGC TTC CAC CAC TTT CCC ATC GAG CGC CAG     192
Ser Leu Val His Asp Val Arg Phe His His Phe Pro Ile Glu Arg Gln
    50                  55                  60

CTC AAC GGC ACC TAC GCC ATT GCC GGC GGC AAA GCG CAC TGT GGA CCG     240
Leu Asn Gly Thr Tyr Ala Ile Ala Gly Gly Lys Ala His Cys Gly Pro
65                  70                  75                  80

GCA GAG CTC TGC GAG TTC TAC TCG CGC GAC CCC GAC GGG CTG CCC TGC     288
Ala Glu Leu Cys Glu Phe Tyr Ser Arg Asp Pro Asp Gly Leu Pro Cys
                85                  90                  95

AAC CTG CGC AAG CCG TGC AAC CGG CCG TCG GGC CTC GAG CCG CAG CCG     336
Asn Leu Arg Lys Pro Cys Asn Arg Pro Ser Gly Leu Glu Pro Gln Pro
            100                 105                 110

GGG GTC TTC GAC TGC CTG CGA GAC GCC ATG GTG CGT GAC TAC GTG CGC     384
Gly Val Phe Asp Cys Leu Arg Asp Ala Met Val Arg Asp Tyr Val Arg
        115                 120                 125

CAG ACG TGG AAG CTG GAG GGC GAG GCC CTG GAG CAG GCC ATC ATC AGC     432
Gln Thr Trp Lys Leu Glu Gly Glu Ala Leu Glu Gln Ala Ile Ile Ser
    130                 135                 140

CAG GCC CCG CAG GTG GAG AAG CTC ATT GCT ACG ACG GCC CAC GAG CGG     480
Gln Ala Pro Gln Val Glu Lys Leu Ile Ala Thr Thr Ala His Glu Arg
145                 150                 155                 160

ATG CCC TGG TAC CAC AGC AGC CTG ACG CGT GAG GAG GCC GAG CGC AAA     528
Met Pro Trp Tyr His Ser Ser Leu Thr Arg Glu Glu Ala Glu Arg Lys
                165                 170                 175

CTT TAC TCT GGG GCG CAG ACC GAC GGC AAG TTC CTG CTG AGG CCG CGG     576
Leu Tyr Ser Gly Ala Gln Thr Asp Gly Lys Phe Leu Leu Arg Pro Arg
            180                 185                 190

AAG GAG CAG GGC ACA TAC GCC CTG TCC CTC ATC TAT GGG AAG ACG GTG     624
Lys Glu Gln Gly Thr Tyr Ala Leu Ser Leu Ile Tyr Gly Lys Thr Val
        195                 200                 205

TAC CAC TAC CTC ATC AGC CAA GAC AAG GCG GGC AAG TAC TGC ATT CCC     672
Tyr His Tyr Leu Ile Ser Gln Asp Lys Ala Gly Lys Tyr Cys Ile Pro
    210                 215                 220
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GAG GGC ACC AAG TTT GAC ACG CTC TGG CAG CTG GTG GAG TAT CTG AAG      720
Glu Gly Thr Lys Phe Asp Thr Leu Trp Gln Leu Val Glu Tyr Leu Lys
225                 230                 235                 240

CTG AAG GCG GAC GGG CTC ATC TAC TGC CTG AAG GAG GCC TGC CCC AAC      768
Leu Lys Ala Asp Gly Leu Ile Tyr Cys Leu Lys Glu Ala Cys Pro Asn
                245                 250                 255

AGC AGT GCC AGC AAC GCC TCA GGG GCT GCT GCT CCC ACA CTC CCA GCC      816
Ser Ser Ala Ser Asn Ala Ser Gly Ala Ala Ala Pro Thr Leu Pro Ala
            260                 265                 270

CAC CCA TCC ACG TTG ACT CAT CCT CAG AGA CGA ATC GAC ACC CTC AAC      864
His Pro Ser Thr Leu Thr His Pro Gln Arg Arg Ile Asp Thr Leu Asn
        275                 280                 285

TCA GAT GGA TAC ACC CCT GAG CCA GCA CGC ATA ACG TCC CCA GAC AAA      912
Ser Asp Gly Tyr Thr Pro Glu Pro Ala Arg Ile Thr Ser Pro Asp Lys
    290                 295                 300

CCG CGG CCG ATG CCC ATG GAC ACG AGC GTG TAT GAG AGC CCC TAC AGC      960
Pro Arg Pro Met Pro Met Asp Thr Ser Val Tyr Glu Ser Pro Tyr Ser
305                 310                 315                 320

GAC CCA GAG GAG CTC AAG GAC AAG AAG CTC TTC CTG AAG CGC GAT AAC     1008
Asp Pro Glu Glu Leu Lys Asp Lys Lys Leu Phe Leu Lys Arg Asp Asn
                325                 330                 335

CTC CTC ATA GCT GAC ATT GAA CTT GGC TGC GGC AAC TTT GGC TCA GTG     1056
Leu Leu Ile Ala Asp Ile Glu Leu Gly Cys Gly Asn Phe Gly Ser Val
            340                 345                 350

CGC CAG GGC GTG TAC CGC ATG CGC AAG AAG CAG ATC GAC GTG GCC ATC     1104
Arg Gln Gly Val Tyr Arg Met Arg Lys Lys Gln Ile Asp Val Ala Ile
        355                 360                 365

AAG GTG CTG AAG CAG GGC ACG GAG AAG GCA GAC ACG GAA GAG ATG ATG     1152
Lys Val Leu Lys Gln Gly Thr Glu Lys Ala Asp Thr Glu Glu Met Met
    370                 375                 380

CGC GAG GCG CAG ATC ATG CAC CAG CTG GAC AAC CCC TAC ATC GTG CGG     1200
Arg Glu Ala Gln Ile Met His Gln Leu Asp Asn Pro Tyr Ile Val Arg
385                 390                 395                 400

CTC ATT GGC GTC TGC CAG GCC GAG GCC CTC ATG CTG GTC ATG GAG ATG     1248
Leu Ile Gly Val Cys Gln Ala Glu Ala Leu Met Leu Val Met Glu Met
                405                 410                 415

GCT GGG GGC GGG CCG CTG CAC AAG TTC CTG GTC GGC AAG AGG GAG GAG     1296
Ala Gly Gly Gly Pro Leu His Lys Phe Leu Val Gly Lys Arg Glu Glu
            420                 425                 430

ATC CCT GTG AGC AAT GTG GCC GAG CTG CTG CAC CAG GTG TCC ATG GGG     1344
Ile Pro Val Ser Asn Val Ala Glu Leu Leu His Gln Val Ser Met Gly
        435                 440                 445
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ATG AAG TAC CTG GAG GAG AAG AAC TTT GTG CAC CGT GAC CTG GCG GCC    1392
Met Lys Tyr Leu Glu Glu Lys Asn Phe Val His Arg Asp Leu Ala Ala
    450                 455                 460

CGC AAC GTC CTG CTG GTT AAC CGG CAC TAC GCC AAG ATC AGC GAC TTT    1440
Arg Asn Val Leu Leu Val Asn Arg His Tyr Ala Lys Ile Ser Asp Phe
465                 470                 475                 480

GGC CTC TCC AAA GCA CTG GGT GCC GAC GAC AGC TAC TAC ACT GCC CGC    1488
Gly Leu Ser Lys Ala Leu Gly Ala Asp Asp Ser Tyr Tyr Thr Ala Arg
                485                 490                 495

TCA GCA GGG AAG TGG CCG CTC AAG TGG TAC GCA CCC GAA TGC ATC AAC    1536
Ser Ala Gly Lys Trp Pro Leu Lys Trp Tyr Ala Pro Glu Cys Ile Asn
            500                 505                 510

TTC CGC AAG TTC TCC AGC CGC AGC GAT GTC TGG AGC TAT GGG GTC ACC    1584
Phe Arg Lys Phe Ser Ser Arg Ser Asp Val Trp Ser Tyr Gly Val Thr
        515                 520                 525

ATG TGG GAG GCC TTG TCC TAC GGC CAG AAG CCC TAC AAG AAG ATG AAA    1632
Met Trp Glu Ala Leu Ser Tyr Gly Gln Lys Pro Tyr Lys Lys Met Lys
    530                 535                 540

GGG CCG GAG GTC ATG GCC TTC ATC GAG CAG GGC AAG CGG ATG GAG TGC    1680
Gly Pro Glu Val Met Ala Phe Ile Glu Gln Gly Lys Arg Met Glu Cys
545                 550                 555                 560

CCA CCA GAG TGT CCA CCC GAA CTG TAC GCA CTC ATG AGT GAC TGC TGG    1728
Pro Pro Glu Cys Pro Pro Glu Leu Tyr Ala Leu Met Ser Asp Cys Trp
                565                 570                 575

ATC TAC AAG TGG GAG GAT CGC CCC GAC TTC CTG ACC GTG GAG CAG CGC    1776
Ile Tyr Lys Trp Glu Asp Arg Pro Asp Phe Leu Thr Val Glu Gln Arg
            580                 585                 590

ATG CGA GCC TGT TAC TAC AGC CTG GCC AGC AAG GTG GAA GGG CCC CCA    1824
Met Arg Ala Cys Tyr Tyr Ser Leu Ala Ser Lys Val Glu Gly Pro Pro
        595                 600                 605

GGC AGC ACA CAG AAG GCT GAG GCT GCC TGT GCC TGG GAT CCA CCG GTC    1872
Gly Ser Thr Gln Lys Ala Glu Ala Ala Cys Ala Trp Asp Pro Pro Val
    610                 615                 620

GCC ACC ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC    1920
Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro
625                 630                 635                 640

ATC CTG GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG    1968
Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val
                645                 650                 655

TCC GGC GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG    2016
Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys
            660                 665                 670
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TTC ATC TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG     2064
Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val
        675                 680                 685

ACC ACC CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC     2112
Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His
    690                 695                 700

ATG AAG CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC     2160
Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val
705                 710                 715                 720

CAG GAG CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC     2208
Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg
                725                 730                 735

GCC GAG GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG     2256
Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu
            740                 745                 750

AAG GGC ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG     2304
Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu
        755                 760                 765

GAG TAC AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG     2352
Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln
    770                 775                 780

AAG AAC GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC     2400
Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp
785                 790                 795                 800

GGC AGC GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC     2448
Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly
                805                 810                 815

GAC GGC CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC     2496
Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser
            820                 825                 830

GCC CTG AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG     2544
Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu
        835                 840                 845

GAG TTC GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC     2592
Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr
    850                 855                 860

AAG TAA                                                             2598
Lys
865
```

(2) INFORMATION FOR SEQ ID NO:111:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 865 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:111:

```
Met Pro Asp Pro Ala Ala His Leu Pro Phe Phe Tyr Gly Ser Ile Ser
 1               5                  10                  15
Arg Ala Glu Ala Glu Glu His Leu Lys Leu Ala Gly Met Ala Asp Gly
            20                  25                  30
Leu Phe Leu Leu Arg Gln Cys Leu Arg Ser Leu Gly Gly Tyr Val Leu
        35                  40                  45
Ser Leu Val His Asp Val Arg Phe His His Phe Pro Ile Glu Arg Gln
    50                  55                  60
Leu Asn Gly Thr Tyr Ala Ile Ala Gly Gly Lys Ala His Cys Gly Pro
65                  70                  75                  80
Ala Glu Leu Cys Glu Phe Tyr Ser Arg Asp Pro Asp Gly Leu Pro Cys
                85                  90                  95
Asn Leu Arg Lys Pro Cys Asn Arg Pro Ser Gly Leu Glu Pro Gln Pro
            100                 105                 110
Gly Val Phe Asp Cys Leu Arg Asp Ala Met Val Arg Asp Tyr Val Arg
        115                 120                 125
Gln Thr Trp Lys Leu Glu Gly Glu Ala Leu Glu Gln Ala Ile Ile Ser
    130                 135                 140
Gln Ala Pro Gln Val Glu Lys Leu Ile Ala Thr Thr Ala His Glu Arg
145                 150                 155                 160
Met Pro Trp Tyr His Ser Ser Leu Thr Arg Glu Glu Ala Glu Arg Lys
                165                 170                 175
Leu Tyr Ser Gly Ala Gln Thr Asp Gly Lys Phe Leu Leu Arg Pro Arg
            180                 185                 190
Lys Glu Gln Gly Thr Tyr Ala Leu Ser Leu Ile Tyr Gly Lys Thr Val
        195                 200                 205
Tyr His Tyr Leu Ile Ser Gln Asp Lys Ala Gly Lys Tyr Cys Ile Pro
    210                 215                 220
Glu Gly Thr Lys Phe Asp Thr Leu Trp Gln Leu Val Glu Tyr Leu Lys
225                 230                 235                 240
Leu Lys Ala Asp Gly Leu Ile Tyr Cys Leu Lys Glu Ala Cys Pro Asn
                245                 250                 255
Ser Ser Ala Ser Asn Ala Ser Gly Ala Ala Ala Pro Thr Leu Pro Ala
            260                 265                 270
His Pro Ser Thr Leu Thr His Pro Gln Arg Arg Ile Asp Thr Leu Asn
        275                 280                 285
Ser Asp Gly Tyr Thr Pro Glu Pro Ala Arg Ile Thr Ser Pro Asp Lys
    290                 295                 300
Pro Arg Pro Met Pro Met Asp Thr Ser Val Tyr Glu Ser Pro Tyr Ser
305                 310                 315                 320
Asp Pro Glu Glu Leu Lys Asp Lys Lys Leu Phe Leu Lys Arg Asp Asn
                325                 330                 335
Leu Leu Ile Ala Asp Ile Glu Leu Gly Cys Gly Asn Phe Gly Ser Val
            340                 345                 350
Arg Gln Gly Val Tyr Arg Met Arg Lys Lys Gln Ile Asp Val Ala Ile
```


BNSDOCID: <WO___9845704A2_I_>

```
          355                 360                 365
Lys Val Leu Lys Gln Gly Thr Glu Lys Ala Asp Thr Glu Glu Met Met
    370                 375                 380
Arg Glu Ala Gln Ile Met His Gln Leu Asp Asn Pro Tyr Ile Val Arg
385                 390                 395                 400
Leu Ile Gly Val Cys Gln Ala Glu Ala Leu Met Leu Val Met Glu Met
                405                 410                 415
Ala Gly Gly Gly Pro Leu His Lys Phe Leu Val Gly Lys Arg Glu Glu
            420                 425                 430
Ile Pro Val Ser Asn Val Ala Glu Leu Leu His Gln Val Ser Met Gly
        435                 440                 445
Met Lys Tyr Leu Glu Glu Lys Asn Phe Val His Arg Asp Leu Ala Ala
    450                 455                 460
Arg Asn Val Leu Leu Val Asn Arg His Tyr Ala Lys Ile Ser Asp Phe
465                 470                 475                 480
Gly Leu Ser Lys Ala Leu Gly Ala Asp Asp Ser Tyr Tyr Thr Ala Arg
                485                 490                 495
Ser Ala Gly Lys Trp Pro Leu Lys Trp Tyr Ala Pro Glu Cys Ile Asn
            500                 505                 510
Phe Arg Lys Phe Ser Ser Arg Ser Asp Val Trp Ser Tyr Gly Val Thr
        515                 520                 525
Met Trp Glu Ala Leu Ser Tyr Gly Gln Lys Pro Tyr Lys Lys Met Lys
    530                 535                 540
Gly Pro Glu Val Met Ala Phe Ile Glu Gln Gly Lys Arg Met Glu Cys
545                 550                 555                 560
Pro Pro Glu Cys Pro Pro Glu Leu Tyr Ala Leu Met Ser Asp Cys Trp
                565                 570                 575
Ile Tyr Lys Trp Glu Asp Arg Pro Asp Phe Leu Thr Val Glu Gln Arg
            580                 585                 590
Met Arg Ala Cys Tyr Tyr Ser Leu Ala Ser Lys Val Glu Gly Pro Pro
        595                 600                 605
Gly Ser Thr Gln Lys Ala Glu Ala Ala Cys Ala Trp Asp Pro Pro Val
    610                 615                 620
Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro
625                 630                 635                 640
Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val
                645                 650                 655
Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys
            660                 665                 670
Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val
        675                 680                 685
Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His
    690                 695                 700
Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val
705                 710                 715                 720
Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg
                725                 730                 735
Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu
            740                 745                 750
Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu
        755                 760                 765
Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln
    770                 775                 780
Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp
785                 790                 795                 800
Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly
```

```
                805                 810                 815
Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser
            820                 825                 830
Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu
        835                 840                 845
Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr
    850                 855                 860
Lys
865
```

(2) INFORMATION FOR SEQ ID NO:112:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1635 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...1632
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:112:

```
ATG GAG AAC TTC CAA AAG GTG GAA AAG ATC GGA GAG GGC ACG TAC GGA      48
Met Glu Asn Phe Gln Lys Val Glu Lys Ile Gly Glu Gly Thr Tyr Gly
 1               5                  10                  15

GTT GTG TAC AAA GCC AGA AAC AAG TTG ACG GGA GAG GTG GTG GCG CTT      96
Val Val Tyr Lys Ala Arg Asn Lys Leu Thr Gly Glu Val Val Ala Leu
            20                  25                  30

AAG AAA ATC CGC CTG GAC ACT GAG ACT GAG GGT GTG CCC AGT ACT GCC     144
Lys Lys Ile Arg Leu Asp Thr Glu Thr Glu Gly Val Pro Ser Thr Ala
        35                  40                  45

ATC CGA GAG ATC TCT CTG CTT AAG GAG CTT AAC CAT CCT AAT ATT GTC     192
Ile Arg Glu Ile Ser Leu Leu Lys Glu Leu Asn His Pro Asn Ile Val
    50                  55                  60

AAG CTG CTG GAT GTC ATT CAC ACA GAA AAT AAA CTC TAC CTG GTT TTT     240
Lys Leu Leu Asp Val Ile His Thr Glu Asn Lys Leu Tyr Leu Val Phe
65                  70                  75                  80

GAA TTT CTG CAC CAA GAT CTC AAG AAA TTC ATG GAT GCC TCT GCT CTC     288
Glu Phe Leu His Gln Asp Leu Lys Lys Phe Met Asp Ala Ser Ala Leu
                85                  90                  95

ACT GGC ATT CCT CTT CCC CTC ATC AAG AGC TAT CTG TTC CAG CTG CTC     336
Thr Gly Ile Pro Leu Pro Leu Ile Lys Ser Tyr Leu Phe Gln Leu Leu
            100                 105                 110

CAG GGC CTA GCT TTC TGC CAT TCT CAT CGG GTC CTC CAC CGA GAC CTT     384
```


BNSDOCID: <WO___9845704A2_I_>

```
Gln Gly Leu Ala Phe Cys His Ser His Arg Val Leu His Arg Asp Leu
        115                 120                 125

AAA CCT CAG AAT CTG CTT ATT AAC ACA GAG GGG GCC ATC AAG CTA GCA  432
Lys Pro Gln Asn Leu Leu Ile Asn Thr Glu Gly Ala Ile Lys Leu Ala
    130                 135                 140

GAC TTT GGA CTA GCC AGA GCT TTT GGA GTC CCT GTT CGT ACT TAC ACC  480
Asp Phe Gly Leu Ala Arg Ala Phe Gly Val Pro Val Arg Thr Tyr Thr
145                 150                 155                 160

CAT GAG GTG GTG ACC CTG TGG TAC CGA GCT CCT GAA ATC CTC CTG GGC  528
His Glu Val Val Thr Leu Trp Tyr Arg Ala Pro Glu Ile Leu Leu Gly
                165                 170                 175

TCG AAA TAT TAT TCC ACA GCT GTG GAC ATC TGG AGC CTG GGC TGC ATC  576
Ser Lys Tyr Tyr Ser Thr Ala Val Asp Ile Trp Ser Leu Gly Cys Ile
            180                 185                 190

TTT GCT GAG ATG GTG ACT CGC CGG GCC CTG TTC CCT GGA GAT TCT GAG  624
Phe Ala Glu Met Val Thr Arg Arg Ala Leu Phe Pro Gly Asp Ser Glu
        195                 200                 205

ATT GAC CAG CTC TTC CGG ATC TTT CGG ACT CTG GGG ACC CCA GAT GAG  672
Ile Asp Gln Leu Phe Arg Ile Phe Arg Thr Leu Gly Thr Pro Asp Glu
    210                 215                 220

GTG GTG TGG CCA GGA GTT ACT TCT ATG CCT GAT TAC AAG CCA AGT TTC  720
Val Val Trp Pro Gly Val Thr Ser Met Pro Asp Tyr Lys Pro Ser Phe
225                 230                 235                 240

CCC AAG TGG GCC CGG CAA GAT TTT AGT AAA GTT GTA CCT CCC CTG GAT  768
Pro Lys Trp Ala Arg Gln Asp Phe Ser Lys Val Val Pro Pro Leu Asp
                245                 250                 255

GAA GAT GGA CGG AGC TTG TTA TCG CAA ATG CTG CAC TAC GAC CCT AAC  816
Glu Asp Gly Arg Ser Leu Leu Ser Gln Met Leu His Tyr Asp Pro Asn
            260                 265                 270

AAG CGG ATT TCG GCC AAG GCA GCC CTG GCT CAC CCT TTC TTC CAG GAT  864
Lys Arg Ile Ser Ala Lys Ala Ala Leu Ala His Pro Phe Phe Gln Asp
        275                 280                 285

GTG ACC AAG CCA GTA CCC CAT CTT CGA CTC TGG GAT CCA CCG GTC GCC  912
Val Thr Lys Pro Val Pro His Leu Arg Leu Trp Asp Pro Pro Val Ala
    290                 295                 300

ACC ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC  960
Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile
305                 310                 315                 320

CTG GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC 1008
Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser
                325                 330                 335

GGC GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC 1056
```


BNSDOCID: <WO___9845704A2_I_>

```
Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe
            340                 345                 350

ATC TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC    1104
Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr
        355                 360                 365

ACC CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG    1152
Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met
    370                 375                 380

AAG CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG    1200
Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln
385                 390                 395                 400

GAG CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC    1248
Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala
                405                 410                 415

GAG GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG    1296
Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys
            420                 425                 430

GGC ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG    1344
Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu
        435                 440                 445

TAC AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG    1392
Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys
    450                 455                 460

AAC GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC    1440
Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly
465                 470                 475                 480

AGC GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC    1488
Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp
                485                 490                 495

GGC CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC    1536
Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala
            500                 505                 510

CTG AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG    1584
Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu
        515                 520                 525

TTC GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG T  1633
Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
    530                 535                 540

AA                                                                 1635
```

(2) INFORMATION FOR SEQ ID NO:113:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 544 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:113:

```
Met Glu Asn Phe Gln Lys Val Glu Lys Ile Gly Glu Gly Thr Tyr Gly
 1               5                  10                  15
Val Val Tyr Lys Ala Arg Asn Lys Leu Thr Gly Glu Val Val Ala Leu
            20                  25                  30
Lys Lys Ile Arg Leu Asp Thr Glu Thr Glu Gly Val Pro Ser Thr Ala
        35                  40                  45
Ile Arg Glu Ile Ser Leu Leu Lys Glu Leu Asn His Pro Asn Ile Val
    50                  55                  60
Lys Leu Leu Asp Val Ile His Thr Glu Asn Lys Leu Tyr Leu Val Phe
65                  70                  75                  80
Glu Phe Leu His Gln Asp Leu Lys Lys Phe Met Asp Ala Ser Ala Leu
                85                  90                  95
Thr Gly Ile Pro Leu Pro Leu Ile Lys Ser Tyr Leu Phe Gln Leu Leu
            100                 105                 110
Gln Gly Leu Ala Phe Cys His Ser His Arg Val Leu His Arg Asp Leu
        115                 120                 125
Lys Pro Gln Asn Leu Leu Ile Asn Thr Glu Gly Ala Ile Lys Leu Ala
    130                 135                 140
Asp Phe Gly Leu Ala Arg Ala Phe Gly Val Pro Val Arg Thr Tyr Thr
145                 150                 155                 160
His Glu Val Val Thr Leu Trp Tyr Arg Ala Pro Glu Ile Leu Leu Gly
                165                 170                 175
Ser Lys Tyr Tyr Ser Thr Ala Val Asp Ile Trp Ser Leu Gly Cys Ile
            180                 185                 190
Phe Ala Glu Met Val Thr Arg Arg Ala Leu Phe Pro Gly Asp Ser Glu
        195                 200                 205
Ile Asp Gln Leu Phe Arg Ile Phe Arg Thr Leu Gly Thr Pro Asp Glu
    210                 215                 220
Val Val Trp Pro Gly Val Thr Ser Met Pro Asp Tyr Lys Pro Ser Phe
225                 230                 235                 240
Pro Lys Trp Ala Arg Gln Asp Phe Ser Lys Val Val Pro Pro Leu Asp
                245                 250                 255
Glu Asp Gly Arg Ser Leu Leu Ser Gln Met Leu His Tyr Asp Pro Asn
            260                 265                 270
Lys Arg Ile Ser Ala Lys Ala Ala Leu Ala His Pro Phe Phe Gln Asp
        275                 280                 285
Val Thr Lys Pro Val Pro His Leu Arg Leu Trp Asp Pro Pro Val Ala
    290                 295                 300
Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile
305                 310                 315                 320
Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser
                325                 330                 335
Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe
            340                 345                 350
Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr
        355                 360                 365
```


BNSDOCID: <WO___9845704A2_I_>

```
Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met
    370                 375                 380
Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln
385                 390                 395                 400
Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala
                405                 410                 415
Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys
            420                 425                 430
Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu
        435                 440                 445
Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys
    450                 455                 460
Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly
465                 470                 475                 480
Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp
                485                 490                 495
Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala
            500                 505                 510
Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu
        515                 520                 525
Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
    530                 535                 540
```

(2) INFORMATION FOR SEQ ID NO:114:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1635 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...1632
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:114:

```
ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15

GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30

GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45

TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC     192
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60
```

```
CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG      240
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80

CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG      288
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95

CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG      336
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110

GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC      384
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125

ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC      432
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140

AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC      480
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160

GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC      528
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175

GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC      576
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190

CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG      624
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205

AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC      672
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220

GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC      720
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240

GGA CTC AGA TCT CGA GCC ATG GAG AAC TTC CAA AAG GTG GAA AAG ATC      768
Gly Leu Arg Ser Arg Ala Met Glu Asn Phe Gln Lys Val Glu Lys Ile
                245                 250                 255

GGA GAG GGC ACG TAC GGA GTT GTG TAC AAA GCC AGA AAC AAG TTG ACG      816
Gly Glu Gly Thr Tyr Gly Val Val Tyr Lys Ala Arg Asn Lys Leu Thr
            260                 265                 270

GGA GAG GTG GTG GCG CTT AAG AAA ATC CGC CTG GAC ACT GAG ACT GAG      864
Gly Glu Val Val Ala Leu Lys Lys Ile Arg Leu Asp Thr Glu Thr Glu
        275                 280                 285
```


BNSDOCID: <WO___9845704A2_I_>

```
GGT GTG CCC AGT ACT GCC ATC CGA GAG ATC TCT CTG CTT AAG GAG CTT      912
Gly Val Pro Ser Thr Ala Ile Arg Glu Ile Ser Leu Leu Lys Glu Leu
    290                 295                 300

AAC CAT CCT AAT ATT GTC AAG CTG CTG GAT GTC ATT CAC ACA GAA AAT      960
Asn His Pro Asn Ile Val Lys Leu Leu Asp Val Ile His Thr Glu Asn
305                 310                 315                 320

AAA CTC TAC CTG GTT TTT GAA TTT CTG CAC CAA GAT CTC AAG AAA TTC     1008
Lys Leu Tyr Leu Val Phe Glu Phe Leu His Gln Asp Leu Lys Lys Phe
                325                 330                 335

ATG GAT GCC TCT GCT CTC ACT GGC ATT CCT CTT CCC CTC ATC AAG AGC     1056
Met Asp Ala Ser Ala Leu Thr Gly Ile Pro Leu Pro Leu Ile Lys Ser
            340                 345                 350

TAT CTG TTC CAG CTG CTC CAG GGC CTA GCT TTC TGC CAT TCT CAT CGG     1104
Tyr Leu Phe Gln Leu Leu Gln Gly Leu Ala Phe Cys His Ser His Arg
        355                 360                 365

GTC CTC CAC CGA GAC CTT AAA CCT CAG AAT CTG CTT ATT AAC ACA GAG     1152
Val Leu His Arg Asp Leu Lys Pro Gln Asn Leu Leu Ile Asn Thr Glu
    370                 375                 380

GGG GCC ATC AAG CTA GCA GAC TTT GGA CTA GCC AGA GCT TTT GGA GTC     1200
Gly Ala Ile Lys Leu Ala Asp Phe Gly Leu Ala Arg Ala Phe Gly Val
385                 390                 395                 400

CCT GTT CGT ACT TAC ACC CAT GAG GTG GTG ACC CTG TGG TAC CGA GCT     1248
Pro Val Arg Thr Tyr Thr His Glu Val Val Thr Leu Trp Tyr Arg Ala
                405                 410                 415

CCT GAA ATC CTC CTG GGC TCG AAA TAT TAT TCC ACA GCT GTG GAC ATC     1296
Pro Glu Ile Leu Leu Gly Ser Lys Tyr Tyr Ser Thr Ala Val Asp Ile
            420                 425                 430

TGG AGC CTG GGC TGC ATC TTT GCT GAG ATG GTG ACT CGC CGG GCC CTG     1344
Trp Ser Leu Gly Cys Ile Phe Ala Glu Met Val Thr Arg Arg Ala Leu
        435                 440                 445

TTC CCT GGA GAT TCT GAG ATT GAC CAG CTC TTC CGG ATC TTT CGG ACT     1392
Phe Pro Gly Asp Ser Glu Ile Asp Gln Leu Phe Arg Ile Phe Arg Thr
    450                 455                 460

CTG GGG ACC CCA GAT GAG GTG GTG TGG CCA GGA GTT ACT TCT ATG CCT     1440
Leu Gly Thr Pro Asp Glu Val Val Trp Pro Gly Val Thr Ser Met Pro
465                 470                 475                 480

GAT TAC AAG CCA AGT TTC CCC AAG TGG GCC CGG CAA GAT TTT AGT AAA     1488
Asp Tyr Lys Pro Ser Phe Pro Lys Trp Ala Arg Gln Asp Phe Ser Lys
                485                 490                 495

GTT GTA CCT CCC CTG GAT GAA GAT GGA CGG AGC TTG TTA TCG CAA ATG     1536
Val Val Pro Pro Leu Asp Glu Asp Gly Arg Ser Leu Leu Ser Gln Met
            500                 505                 510
```

```
CTG CAC TAC GAC CCT AAC AAG CGG ATT TCG GCC AAG GCA GCC CTG GCT     1584
Leu His Tyr Asp Pro Asn Lys Arg Ile Ser Ala Lys Ala Ala Leu Ala
        515                 520                 525

CAC CCT TTC TTC CAG GAT GTG ACC AAG CCA GTA CCC CAT CTT CGA CTC T  1633
His Pro Phe Phe Gln Asp Val Thr Lys Pro Val Pro His Leu Arg Leu
    530                 535                 540

GA                                                                 1635
```

(2) INFORMATION FOR SEQ ID NO:115:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 544 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:115:

```
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240
Gly Leu Arg Ser Arg Ala Met Glu Asn Phe Gln Lys Val Glu Lys Ile
                245                 250                 255
Gly Glu Gly Thr Tyr Gly Val Val Tyr Lys Ala Arg Asn Lys Leu Thr
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                260                 265                 270
Gly Glu Val Val Ala Leu Lys Lys Ile Arg Leu Asp Thr Glu Thr Glu
        275                 280                 285
Gly Val Pro Ser Thr Ala Ile Arg Glu Ile Ser Leu Leu Lys Glu Leu
    290                 295                 300
Asn His Pro Asn Ile Val Lys Leu Leu Asp Val Ile His Thr Glu Asn
305                 310                 315                 320
Lys Leu Tyr Leu Val Phe Glu Phe Leu His Gln Asp Leu Lys Lys Phe
                325                 330                 335
Met Asp Ala Ser Ala Leu Thr Gly Ile Pro Leu Pro Leu Ile Lys Ser
            340                 345                 350
Tyr Leu Phe Gln Leu Leu Gln Gly Leu Ala Phe Cys His Ser His Arg
        355                 360                 365
Val Leu His Arg Asp Leu Lys Pro Gln Asn Leu Leu Ile Asn Thr Glu
    370                 375                 380
Gly Ala Ile Lys Leu Ala Asp Phe Gly Leu Ala Arg Ala Phe Gly Val
385                 390                 395                 400
Pro Val Arg Thr Tyr Thr His Glu Val Val Thr Leu Trp Tyr Arg Ala
                405                 410                 415
Pro Glu Ile Leu Leu Gly Ser Lys Tyr Tyr Ser Thr Ala Val Asp Ile
            420                 425                 430
Trp Ser Leu Gly Cys Ile Phe Ala Glu Met Val Thr Arg Arg Ala Leu
        435                 440                 445
Phe Pro Gly Asp Ser Glu Ile Asp Gln Leu Phe Arg Ile Phe Arg Thr
    450                 455                 460
Leu Gly Thr Pro Asp Glu Val Val Trp Pro Gly Val Thr Ser Met Pro
465                 470                 475                 480
Asp Tyr Lys Pro Ser Phe Pro Lys Trp Ala Arg Gln Asp Phe Ser Lys
                485                 490                 495
Val Val Pro Pro Leu Asp Glu Asp Gly Arg Ser Leu Leu Ser Gln Met
            500                 505                 510
Leu His Tyr Asp Pro Asn Lys Arg Ile Ser Ala Lys Ala Ala Leu Ala
        515                 520                 525
His Pro Phe Phe Gln Asp Val Thr Lys Pro Val Pro His Leu Arg Leu
    530                 535                 540
```

(2) INFORMATION FOR SEQ ID NO:116:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2532 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...2529
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:116:

```
ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15
```

```
GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30

GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45

TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC     192
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60

CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG     240
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80

CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG     288
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95

CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG     336
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110

GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC     384
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125

ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC     432
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140

AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC     480
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160

GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC     528
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175

GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC     576
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190

CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG     624
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205

AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC     672
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220

GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC     720
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240
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GGA CTC AGA TCT CGA GAG ATG CTG TCC CGT GGG TGG TTT CAC CGA GAC     768
Gly Leu Arg Ser Arg Glu Met Leu Ser Arg Gly Trp Phe His Arg Asp
                245                 250                 255

CTC AGT GGG CTG GAT GCA GAG ACC CTG CTC AAG GGC CGA GGT GTC CAC     816
Leu Ser Gly Leu Asp Ala Glu Thr Leu Leu Lys Gly Arg Gly Val His
            260                 265                 270

GGT AGC TTC CTG GCT CGG CCC AGT CGC AAG AAC CAG GGT GAC TTC TCG     864
Gly Ser Phe Leu Ala Arg Pro Ser Arg Lys Asn Gln Gly Asp Phe Ser
        275                 280                 285

CTC TCC GTC AGG GTG GGG GAT CAG GTG ACC CAT ATT CGG ATC CAG AAC     912
Leu Ser Val Arg Val Gly Asp Gln Val Thr His Ile Arg Ile Gln Asn
    290                 295                 300

TCA GGG GAT TTC TAT GAC CTG TAT GGA GGG GAG AAG TTT GCG ACT CTG     960
Ser Gly Asp Phe Tyr Asp Leu Tyr Gly Gly Glu Lys Phe Ala Thr Leu
305                 310                 315                 320

ACA GAG CTG GTG GAG TAC TAC ACT CAG CAG CAG GGT GTC CTG CAG GAC    1008
Thr Glu Leu Val Glu Tyr Tyr Thr Gln Gln Gln Gly Val Leu Gln Asp
                325                 330                 335

CGC GAC GGC ACC ATC ATC CAC CTC AAG TAC CCG CTG AAC TGC TCC GAT    1056
Arg Asp Gly Thr Ile Ile His Leu Lys Tyr Pro Leu Asn Cys Ser Asp
            340                 345                 350

CCC ACT AGT GAG AGG TGG TAC CAT GGC CAC ATG TCT GGC GGG CAG GCA    1104
Pro Thr Ser Glu Arg Trp Tyr His Gly His Met Ser Gly Gly Gln Ala
        355                 360                 365

GAG ACG CTG CTG CAG GCC AAG GGC GAG CCC TGG ACG TTT CTT GTG CGT    1152
Glu Thr Leu Leu Gln Ala Lys Gly Glu Pro Trp Thr Phe Leu Val Arg
    370                 375                 380

GAG AGC CTC AGC CAG CCT GGA GAC TTC GTG CTT TCT GTG CTC AGT GAC    1200
Glu Ser Leu Ser Gln Pro Gly Asp Phe Val Leu Ser Val Leu Ser Asp
385                 390                 395                 400

CAG CCC AAG GCT GGC CCA GGC TCC CCG CTC AGG GTC ACC CAC ATC AAG    1248
Gln Pro Lys Ala Gly Pro Gly Ser Pro Leu Arg Val Thr His Ile Lys
                405                 410                 415

GTC ATG TGC GAG GGT GGA CGC TAC ACA GTG GGT GGT TTG GAG ACC TTC    1296
Val Met Cys Glu Gly Gly Arg Tyr Thr Val Gly Gly Leu Glu Thr Phe
            420                 425                 430

GAC AGC CTC ACG GAC CTG GTA GAG CAT TTC AAG AAG ACG GGG ATT GAG    1344
Asp Ser Leu Thr Asp Leu Val Glu His Phe Lys Lys Thr Gly Ile Glu
        435                 440                 445

GAG GCC TCA GGC GCC TTT GTC TAC CTG CGG CAG CCG TAC TAT GCC ACG    1392
Glu Ala Ser Gly Ala Phe Val Tyr Leu Arg Gln Pro Tyr Tyr Ala Thr
    450                 455                 460
```

```
AGG GTG AAT GCG GCT GAC ATT GAG AAC CGA GTG TTG GAA CTG AAC AAG    1440
Arg Val Asn Ala Ala Asp Ile Glu Asn Arg Val Leu Glu Leu Asn Lys
465                 470                 475                 480

AAG CAG GAG TCC GAG GAT ACA GCC AAG GCT GGC TTC TGG GAG GAG TTT    1488
Lys Gln Glu Ser Glu Asp Thr Ala Lys Ala Gly Phe Trp Glu Glu Phe
                485                 490                 495

GAG AGT TTG CAG AAG CAG GAG GTG AAG AAC TTG CAC CAG CGT CTG GAA    1536
Glu Ser Leu Gln Lys Gln Glu Val Lys Asn Leu His Gln Arg Leu Glu
            500                 505                 510

GGG CAG CGG CCA GAG AAC AAG GGC AAG AAC CGC TAC AAG AAC ATT CTC    1584
Gly Gln Arg Pro Glu Asn Lys Gly Lys Asn Arg Tyr Lys Asn Ile Leu
        515                 520                 525

CCC TTT GAC CAC AGC CGA GTG ATC CTG CAG GGA CGG GAC AGT AAC ATC    1632
Pro Phe Asp His Ser Arg Val Ile Leu Gln Gly Arg Asp Ser Asn Ile
    530                 535                 540

CCC GGG TCC GAC TAC ATC AAT GCC AAC TAC ATC AAG AAC CAG CTG CTA    1680
Pro Gly Ser Asp Tyr Ile Asn Ala Asn Tyr Ile Lys Asn Gln Leu Leu
545                 550                 555                 560

GGC CCT GAT GAG AAC GCT AAG ACC TAC ATC GCC AGC CAG GGC TGT CTG    1728
Gly Pro Asp Glu Asn Ala Lys Thr Tyr Ile Ala Ser Gln Gly Cys Leu
                565                 570                 575

GAG GCC ACG GTC AAT GAC TTC TGG CAG ATG GCG TGG CAG GAG AAC AGC    1776
Glu Ala Thr Val Asn Asp Phe Trp Gln Met Ala Trp Gln Glu Asn Ser
            580                 585                 590

CGT GTC ATC GTC ATG ACC ACC CGA GAG GTG GAG AAA GGC CGG AAC AAA    1824
Arg Val Ile Val Met Thr Thr Arg Glu Val Glu Lys Gly Arg Asn Lys
        595                 600                 605

TGC GTC CCA TAC TGG CCC GAG GTG GGC ATG CAG CGT GCT TAT GGG CCC    1872
Cys Val Pro Tyr Trp Pro Glu Val Gly Met Gln Arg Ala Tyr Gly Pro
    610                 615                 620

TAC TCT GTG ACC AAC TGC GGG GAG CAT GAC ACA ACC GAA TAC AAA CTC    1920
Tyr Ser Val Thr Asn Cys Gly Glu His Asp Thr Thr Glu Tyr Lys Leu
625                 630                 635                 640

CGT ACC TTA CAG GTC TCC CCG CTG GAC AAT GGA GAC CTG ATT CGG GAG    1968
Arg Thr Leu Gln Val Ser Pro Leu Asp Asn Gly Asp Leu Ile Arg Glu
                645                 650                 655

ATC TGG CAT TAC CAG TAC CTG AGC TGG CCC GAC CAT GGG GTC CCC AGT    2016
Ile Trp His Tyr Gln Tyr Leu Ser Trp Pro Asp His Gly Val Pro Ser
            660                 665                 670

GAG CCT GGG GGT GTC CTC AGC TTC CTG GAC CAG ATC AAC CAG CGG CAG    2064
Glu Pro Gly Gly Val Leu Ser Phe Leu Asp Gln Ile Asn Gln Arg Gln
        675                 680                 685
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```
GAA AGT CTG CCT CAC GCA GGG CCC ATC ATC GTG CAC TGC AGC GCC GGC    2112
Glu Ser Leu Pro His Ala Gly Pro Ile Ile Val His Cys Ser Ala Gly
    690                 695                 700

ATC GGC CGC ACA GGC ACC ATC ATT GTC ATC GAC ATG CTC ATG GAG AAC    2160
Ile Gly Arg Thr Gly Thr Ile Ile Val Ile Asp Met Leu Met Glu Asn
705                 710                 715                 720

ATC TCC ACC AAG GGC CTG GAC TGT GAC ATT GAC ATC CAG AAG ACC ATC    2208
Ile Ser Thr Lys Gly Leu Asp Cys Asp Ile Asp Ile Gln Lys Thr Ile
                725                 730                 735

CAG ATG GTG CGG GCG CAG CGC TCG GGC ATG GTG CAG ACG GAG GCG CAG    2256
Gln Met Val Arg Ala Gln Arg Ser Gly Met Val Gln Thr Glu Ala Gln
            740                 745                 750

TAC AAG TTC ATC TAC GTG GCC ATC GCC CAG TTC ATT GAA ACC ACT AAG    2304
Tyr Lys Phe Ile Tyr Val Ala Ile Ala Gln Phe Ile Glu Thr Thr Lys
        755                 760                 765

AAG AAG CTG GAG GTC CTG CAG TCG CAG AAG GGC CAG GAG TCG GAG TAC    2352
Lys Lys Leu Glu Val Leu Gln Ser Gln Lys Gly Gln Glu Ser Glu Tyr
    770                 775                 780

GGG AAC ATC ACC TAT CCC CCA GCC ATG AAG AAT GCC CAT GCC AAG GCC    2400
Gly Asn Ile Thr Tyr Pro Pro Ala Met Lys Asn Ala His Ala Lys Ala
785                 790                 795                 800

TCC CGC ACC TCG TCC AAA CAC AAG GAG GAT GTG TAT GAG AAC CTG CAC    2448
Ser Arg Thr Ser Ser Lys His Lys Glu Asp Val Tyr Glu Asn Leu His
                805                 810                 815

ACT AAG AAC AAG AGG GAG GAG AAA GTG AAG AAG CAG CGG TCA GCA GAC    2496
Thr Lys Asn Lys Arg Glu Glu Lys Val Lys Lys Gln Arg Ser Ala Asp
            820                 825                 830

AAG GAG AAG AGC AAG GGT TCC CTC AAG AGG AAG TGA                    2532
Lys Glu Lys Ser Lys Gly Ser Leu Lys Arg Lys
        835                 840
```

(2) INFORMATION FOR SEQ ID NO:117:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 843 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:117:

```
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
```

218

```
 1               5                  10                  15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240
Gly Leu Arg Ser Arg Glu Met Leu Ser Arg Gly Trp Phe His Arg Asp
                245                 250                 255
Leu Ser Gly Leu Asp Ala Glu Thr Leu Leu Lys Gly Arg Gly Val His
            260                 265                 270
Gly Ser Phe Leu Ala Arg Pro Ser Arg Lys Asn Gln Gly Asp Phe Ser
        275                 280                 285
Leu Ser Val Arg Val Gly Asp Gln Val Thr His Ile Arg Ile Gln Asn
    290                 295                 300
Ser Gly Asp Phe Tyr Asp Leu Tyr Gly Gly Glu Lys Phe Ala Thr Leu
305                 310                 315                 320
Thr Glu Leu Val Glu Tyr Tyr Thr Gln Gln Gln Gly Val Leu Gln Asp
                325                 330                 335
Arg Asp Gly Thr Ile Ile His Leu Lys Tyr Pro Leu Asn Cys Ser Asp
            340                 345                 350
Pro Thr Ser Glu Arg Trp Tyr His Gly His Met Ser Gly Gly Gln Ala
        355                 360                 365
Glu Thr Leu Leu Gln Ala Lys Gly Glu Pro Trp Thr Phe Leu Val Arg
    370                 375                 380
Glu Ser Leu Ser Gln Pro Gly Asp Phe Val Leu Ser Val Leu Ser Asp
385                 390                 395                 400
Gln Pro Lys Ala Gly Pro Gly Ser Pro Leu Arg Val Thr His Ile Lys
                405                 410                 415
Val Met Cys Glu Gly Gly Arg Tyr Thr Val Gly Gly Leu Glu Thr Phe
            420                 425                 430
Asp Ser Leu Thr Asp Leu Val Glu His Phe Lys Lys Thr Gly Ile Glu
        435                 440                 445
Glu Ala Ser Gly Ala Phe Val Tyr Leu Arg Gln Pro Tyr Tyr Ala Thr
```


BNSDOCID: <WO___9845704A2_I_>

```
    450                 455                 460
Arg Val Asn Ala Ala Asp Ile Glu Asn Arg Val Leu Glu Leu Asn Lys
465                 470                 475                 480
Lys Gln Glu Ser Glu Asp Thr Ala Lys Ala Gly Phe Trp Glu Glu Phe
                485                 490                 495
Glu Ser Leu Gln Lys Gln Glu Val Lys Asn Leu His Gln Arg Leu Glu
            500                 505                 510
Gly Gln Arg Pro Glu Asn Lys Gly Lys Asn Arg Tyr Lys Asn Ile Leu
        515                 520                 525
Pro Phe Asp His Ser Arg Val Ile Leu Gln Gly Arg Asp Ser Asn Ile
    530                 535                 540
Pro Gly Ser Asp Tyr Ile Asn Ala Asn Tyr Ile Lys Asn Gln Leu Leu
545                 550                 555                 560
Gly Pro Asp Glu Asn Ala Lys Thr Tyr Ile Ala Ser Gln Gly Cys Leu
                565                 570                 575
Glu Ala Thr Val Asn Asp Phe Trp Gln Met Ala Trp Gln Glu Asn Ser
            580                 585                 590
Arg Val Ile Val Met Thr Thr Arg Glu Val Glu Lys Gly Arg Asn Lys
        595                 600                 605
Cys Val Pro Tyr Trp Pro Glu Val Gly Met Gln Arg Ala Tyr Gly Pro
    610                 615                 620
Tyr Ser Val Thr Asn Cys Gly Glu His Asp Thr Thr Glu Tyr Lys Leu
625                 630                 635                 640
Arg Thr Leu Gln Val Ser Pro Leu Asp Asn Gly Asp Leu Ile Arg Glu
                645                 650                 655
Ile Trp His Tyr Gln Tyr Leu Ser Trp Pro Asp His Gly Val Pro Ser
            660                 665                 670
Glu Pro Gly Gly Val Leu Ser Phe Leu Asp Gln Ile Asn Gln Arg Gln
        675                 680                 685
Glu Ser Leu Pro His Ala Gly Pro Ile Ile Val His Cys Ser Ala Gly
    690                 695                 700
Ile Gly Arg Thr Gly Thr Ile Ile Val Ile Asp Met Leu Met Glu Asn
705                 710                 715                 720
Ile Ser Thr Lys Gly Leu Asp Cys Asp Ile Asp Ile Gln Lys Thr Ile
                725                 730                 735
Gln Met Val Arg Ala Gln Arg Ser Gly Met Val Gln Thr Glu Ala Gln
            740                 745                 750
Tyr Lys Phe Ile Tyr Val Ala Ile Ala Gln Phe Ile Glu Thr Thr Lys
        755                 760                 765
Lys Lys Leu Glu Val Leu Gln Ser Gln Lys Gly Gln Glu Ser Glu Tyr
    770                 775                 780
Gly Asn Ile Thr Tyr Pro Pro Ala Met Lys Asn Ala His Ala Lys Ala
785                 790                 795                 800
Ser Arg Thr Ser Ser Lys His Lys Glu Asp Val Tyr Glu Asn Leu His
                805                 810                 815
Thr Lys Asn Lys Arg Glu Glu Lys Val Lys Lys Gln Arg Ser Ala Asp
            820                 825                 830
Lys Glu Lys Ser Lys Gly Ser Leu Lys Arg Lys
        835                 840
```

(2) INFORMATION FOR SEQ ID NO:118:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2562 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...2559
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:118:

```
ATG CTG TCC CGT GGG TGG TTT CAC CGA GAC CTC AGT GGG CTG GAT GCA      48
Met Leu Ser Arg Gly Trp Phe His Arg Asp Leu Ser Gly Leu Asp Ala
 1               5                  10                  15

GAG ACC CTG CTC AAG GGC CGA GGT GTC CAC GGT AGC TTC CTG GCT CGG      96
Glu Thr Leu Leu Lys Gly Arg Gly Val His Gly Ser Phe Leu Ala Arg
            20                  25                  30

CCC AGT CGC AAG AAC CAG GGT GAC TTC TCG CTC TCC GTC AGG GTG GGG     144
Pro Ser Arg Lys Asn Gln Gly Asp Phe Ser Leu Ser Val Arg Val Gly
        35                  40                  45

GAT CAG GTG ACC CAT ATT CGG ATC CAG AAC TCA GGG GAT TTC TAT GAC     192
Asp Gln Val Thr His Ile Arg Ile Gln Asn Ser Gly Asp Phe Tyr Asp
    50                  55                  60

CTG TAT GGA GGG GAG AAG TTT GCG ACT CTG ACA GAG CTG GTG GAG TAC     240
Leu Tyr Gly Gly Glu Lys Phe Ala Thr Leu Thr Glu Leu Val Glu Tyr
65                  70                  75                  80

TAC ACT CAG CAG CAG GGT GTC CTG CAG GAC CGC GAC GGC ACC ATC ATC     288
Tyr Thr Gln Gln Gln Gly Val Leu Gln Asp Arg Asp Gly Thr Ile Ile
                85                  90                  95

CAC CTC AAG TAC CCG CTG AAC TGC TCC GAT CCC ACT AGT GAG AGG TGG     336
His Leu Lys Tyr Pro Leu Asn Cys Ser Asp Pro Thr Ser Glu Arg Trp
            100                 105                 110

TAC CAT GGC CAC ATG TCT GGC GGG CAG GCA GAG ACG CTG CTG CAG GCC     384
Tyr His Gly His Met Ser Gly Gly Gln Ala Glu Thr Leu Leu Gln Ala
        115                 120                 125

AAG GGC GAG CCC TGG ACG TTT CTT GTG CGT GAG AGC CTC AGC CAG CCT     432
Lys Gly Glu Pro Trp Thr Phe Leu Val Arg Glu Ser Leu Ser Gln Pro
    130                 135                 140

GGA GAC TTC GTG CTT TCT GTG CTC AGT GAC CAG CCC AAG GCT GGC CCA     480
Gly Asp Phe Val Leu Ser Val Leu Ser Asp Gln Pro Lys Ala Gly Pro
145                 150                 155                 160

GGC TCC CCG CTC AGG GTC ACC CAC ATC AAG GTC ATG TGC GAG GGT GGA     528
Gly Ser Pro Leu Arg Val Thr His Ile Lys Val Met Cys Glu Gly Gly
                165                 170                 175

CGC TAC ACA GTG GGT GGT TTG GAG ACC TTC GAC AGC CTC ACG GAC CTG     576
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```
Arg Tyr Thr Val Gly Gly Leu Glu Thr Phe Asp Ser Leu Thr Asp Leu
            180                 185                 190

GTA GAG CAT TTC AAG AAG ACG GGG ATT GAG GAG GCC TCA GGC GCC TTT     624
Val Glu His Phe Lys Lys Thr Gly Ile Glu Glu Ala Ser Gly Ala Phe
        195                 200                 205

GTC TAC CTG CGG CAG CCG TAC TAT GCC ACG AGG GTG AAT GCG GCT GAC     672
Val Tyr Leu Arg Gln Pro Tyr Tyr Ala Thr Arg Val Asn Ala Ala Asp
    210                 215                 220

ATT GAG AAC CGA GTG TTG GAA CTG AAC AAG AAG CAG GAG TCC GAG GAT     720
Ile Glu Asn Arg Val Leu Glu Leu Asn Lys Lys Gln Glu Ser Glu Asp
225                 230                 235                 240

ACA GCC AAG GCT GGC TTC TGG GAG GAG TTT GAG AGT TTG CAG AAG CAG     768
Thr Ala Lys Ala Gly Phe Trp Glu Glu Phe Glu Ser Leu Gln Lys Gln
                245                 250                 255

GAG GTG AAG AAC TTG CAC CAG CGT CTG GAA GGG CAG CGG CCA GAG AAC     816
Glu Val Lys Asn Leu His Gln Arg Leu Glu Gly Gln Arg Pro Glu Asn
            260                 265                 270

AAG GGC AAG AAC CGC TAC AAG AAC ATT CTC CCC TTT GAC CAC AGC CGA     864
Lys Gly Lys Asn Arg Tyr Lys Asn Ile Leu Pro Phe Asp His Ser Arg
        275                 280                 285

GTG ATC CTG CAG GGA CGG GAC AGT AAC ATC CCC GGG TCC GAC TAC ATC     912
Val Ile Leu Gln Gly Arg Asp Ser Asn Ile Pro Gly Ser Asp Tyr Ile
    290                 295                 300

AAT GCC AAC TAC ATC AAG AAC CAG CTG CTA GGC CCT GAT GAG AAC GCT     960
Asn Ala Asn Tyr Ile Lys Asn Gln Leu Leu Gly Pro Asp Glu Asn Ala
305                 310                 315                 320

AAG ACC TAC ATC GCC AGC CAG GGC TGT CTG GAG GCC ACG GTC AAT GAC    1008
Lys Thr Tyr Ile Ala Ser Gln Gly Cys Leu Glu Ala Thr Val Asn Asp
                325                 330                 335

TTC TGG CAG ATG GCG TGG CAG GAG AAC AGC CGT GTC ATC GTC ATG ACC    1056
Phe Trp Gln Met Ala Trp Gln Glu Asn Ser Arg Val Ile Val Met Thr
            340                 345                 350

ACC CGA GAG GTG GAG AAA GGC CGG AAC AAA TGC GTC CCA TAC TGG CCC    1104
Thr Arg Glu Val Glu Lys Gly Arg Asn Lys Cys Val Pro Tyr Trp Pro
        355                 360                 365

GAG GTG GGC ATG CAG CGT GCT TAT GGG CCC TAC TCT GTG ACC AAC TGC    1152
Glu Val Gly Met Gln Arg Ala Tyr Gly Pro Tyr Ser Val Thr Asn Cys
    370                 375                 380

GGG GAG CAT GAC ACA ACC GAA TAC AAA CTC CGT ACC TTA CAG GTC TCC    1200
Gly Glu His Asp Thr Thr Glu Tyr Lys Leu Arg Thr Leu Gln Val Ser
385                 390                 395                 400

CCG CTG GAC AAT GGA GAC CTG ATT CGG GAG ATC TGG CAT TAC CAG TAC    1248
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```
Pro Leu Asp Asn Gly Asp Leu Ile Arg Glu Ile Trp His Tyr Gln Tyr
                405                 410                 415

CTG AGC TGG CCC GAC CAT GGG GTC CCC AGT GAG CCT GGG GGT GTC CTC    1296
Leu Ser Trp Pro Asp His Gly Val Pro Ser Glu Pro Gly Gly Val Leu
            420                 425                 430

AGC TTC CTG GAC CAG ATC AAC CAG CGG CAG GAA AGT CTG CCT CAC GCA    1344
Ser Phe Leu Asp Gln Ile Asn Gln Arg Gln Glu Ser Leu Pro His Ala
        435                 440                 445

GGG CCC ATC ATC GTG CAC TGC AGC GCC GGC ATC GGC CGC ACA GGC ACC    1392
Gly Pro Ile Ile Val His Cys Ser Ala Gly Ile Gly Arg Thr Gly Thr
    450                 455                 460

ATC ATT GTC ATC GAC ATG CTC ATG GAG AAC ATC TCC ACC AAG GGC CTG    1440
Ile Ile Val Ile Asp Met Leu Met Glu Asn Ile Ser Thr Lys Gly Leu
465                 470                 475                 480

GAC TGT GAC ATT GAC ATC CAG AAG ACC ATC CAG ATG GTG CGG GCG CAG    1488
Asp Cys Asp Ile Asp Ile Gln Lys Thr Ile Gln Met Val Arg Ala Gln
                485                 490                 495

CGC TCG GGC ATG GTG CAG ACG GAG GCG CAG TAC AAG TTC ATC TAC GTG    1536
Arg Ser Gly Met Val Gln Thr Glu Ala Gln Tyr Lys Phe Ile Tyr Val
            500                 505                 510

GCC ATC GCC CAG TTC ATT GAA ACC ACT AAG AAG AAG CTG GAG GTC CTG    1584
Ala Ile Ala Gln Phe Ile Glu Thr Thr Lys Lys Lys Leu Glu Val Leu
        515                 520                 525

CAG TCG CAG AAG GGC CAG GAG TCG GAG TAC GGG AAC ATC ACC TAT CCC    1632
Gln Ser Gln Lys Gly Gln Glu Ser Glu Tyr Gly Asn Ile Thr Tyr Pro
    530                 535                 540

CCA GCC ATG AAG AAT GCC CAT GCC AAG GCC TCC CGC ACC TCG TCC AAA    1680
Pro Ala Met Lys Asn Ala His Ala Lys Ala Ser Arg Thr Ser Ser Lys
545                 550                 555                 560

CAC AAG GAG GAT GTG TAT GAG AAC CTG CAC ACT AAG AAC AAG AGG GAG    1728
His Lys Glu Asp Val Tyr Glu Asn Leu His Thr Lys Asn Lys Arg Glu
                565                 570                 575

GAG AAA GTG AAG AAG CAG CGG TCA GCA GAC AAG GAG AAG AGC AAG GGT    1776
Glu Lys Val Lys Lys Gln Arg Ser Ala Asp Lys Glu Lys Ser Lys Gly
            580                 585                 590

TCC CTC AAG AGG AAG CGA ATT CTG CAG TCG ACG GTA CCG CGG GCC CGG    1824
Ser Leu Lys Arg Lys Arg Ile Leu Gln Ser Thr Val Pro Arg Ala Arg
        595                 600                 605

GAT CCA CCG GTC GCC ACC ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC    1872
Asp Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr
    610                 615                 620

GGG GTG GTG CCC ATC CTG GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC    1920
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Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His
625                 630                 635                 640

AAG TTC AGC GTG TCC GGC GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG    1968
Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys
                645                 650                 655

CTG ACC CTG AAG TTC ATC TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG    2016
Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp
            660                 665                 670

CCC ACC CTC GTG ACC ACC CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC    2064
Pro Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg
        675                 680                 685

TAC CCC GAC CAC ATG AAG CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC    2112
Tyr Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro
    690                 695                 700

GAA GGC TAC GTC CAG GAG CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC    2160
Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn
705                 710                 715                 720

TAC AAG ACC CGC GCC GAG GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC    2208
Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn
                725                 730                 735

CGC ATC GAG CTG AAG GGC ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG    2256
Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu
            740                 745                 750

GGG CAC AAG CTG GAG TAC AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG    2304
Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met
        755                 760                 765

GCC GAC AAG CAG AAG AAC GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC    2352
Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His
    770                 775                 780

AAC ATC GAG GAC GGC AGC GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC    2400
Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn
785                 790                 795                 800

ACC CCC ATC GGC GAC GGC CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG    2448
Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu
                805                 810                 815

AGC ACC CAG TCC GCC CTG AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC    2496
Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His
            820                 825                 830

ATG GTC CTG CTG GAG TTC GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG    2544
Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met
        835                 840                 845

GAC GAG CTG TAC AAG TAA                                            2562
```


BNSDOCID: <WO___9845704A2_I_>

Asp Glu Leu Tyr Lys
850

(2) INFORMATION FOR SEQ ID NO:119:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 853 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:119:

Met Leu Ser Arg Gly Trp Phe His Arg Asp Leu Ser Gly Leu Asp Ala
1 5 10 15
Glu Thr Leu Leu Lys Gly Arg Gly Val His Gly Ser Phe Leu Ala Arg
20 25 30
Pro Ser Arg Lys Asn Gln Gly Asp Phe Ser Leu Ser Val Arg Val Gly
35 40 45
Asp Gln Val Thr His Ile Arg Ile Gln Asn Ser Gly Asp Phe Tyr Asp
50 55 60
Leu Tyr Gly Gly Glu Lys Phe Ala Thr Leu Thr Glu Leu Val Glu Tyr
65 70 75 80
Tyr Thr Gln Gln Gln Gly Val Leu Gln Asp Arg Asp Gly Thr Ile Ile
85 90 95
His Leu Lys Tyr Pro Leu Asn Cys Ser Asp Pro Thr Ser Glu Arg Trp
100 105 110
Tyr His Gly His Met Ser Gly Gly Gln Ala Glu Thr Leu Leu Gln Ala
115 120 125
Lys Gly Glu Pro Trp Thr Phe Leu Val Arg Glu Ser Leu Ser Gln Pro
130 135 140
Gly Asp Phe Val Leu Ser Val Leu Ser Asp Gln Pro Lys Ala Gly Pro
145 150 155 160
Gly Ser Pro Leu Arg Val Thr His Ile Lys Val Met Cys Glu Gly Gly
165 170 175
Arg Tyr Thr Val Gly Gly Leu Glu Thr Phe Asp Ser Leu Thr Asp Leu
180 185 190
Val Glu His Phe Lys Lys Thr Gly Ile Glu Glu Ala Ser Gly Ala Phe
195 200 205
Val Tyr Leu Arg Gln Pro Tyr Tyr Ala Thr Arg Val Asn Ala Ala Asp
210 215 220
Ile Glu Asn Arg Val Leu Glu Leu Asn Lys Lys Gln Glu Ser Glu Asp
225 230 235 240
Thr Ala Lys Ala Gly Phe Trp Glu Glu Phe Glu Ser Leu Gln Lys Gln
245 250 255
Glu Val Lys Asn Leu His Gln Arg Leu Glu Gly Gln Arg Pro Glu Asn
260 265 270
Lys Gly Lys Asn Arg Tyr Lys Asn Ile Leu Pro Phe Asp His Ser Arg
275 280 285
Val Ile Leu Gln Gly Arg Asp Ser Asn Ile Pro Gly Ser Asp Tyr Ile
290 295 300
Asn Ala Asn Tyr Ile Lys Asn Gln Leu Leu Gly Pro Asp Glu Asn Ala

305 310 315 320
Lys Thr Tyr Ile Ala Ser Gln Gly Cys Leu Glu Ala Thr Val Asn Asp
325 330 335
Phe Trp Gln Met Ala Trp Gln Glu Asn Ser Arg Val Ile Val Met Thr
340 345 350
Thr Arg Glu Val Glu Lys Gly Arg Asn Lys Cys Val Pro Tyr Trp Pro
355 360 365
Glu Val Gly Met Gln Arg Ala Tyr Gly Pro Tyr Ser Val Thr Asn Cys
370 375 380
Gly Glu His Asp Thr Thr Glu Tyr Lys Leu Arg Thr Leu Gln Val Ser
385 390 395 400
Pro Leu Asp Asn Gly Asp Leu Ile Arg Glu Ile Trp His Tyr Gln Tyr
405 410 415
Leu Ser Trp Pro Asp His Gly Val Pro Ser Glu Pro Gly Gly Val Leu
420 425 430
Ser Phe Leu Asp Gln Ile Asn Gln Arg Gln Glu Ser Leu Pro His Ala
435 440 445
Gly Pro Ile Ile Val His Cys Ser Ala Gly Ile Gly Arg Thr Gly Thr
450 455 460
Ile Ile Val Ile Asp Met Leu Met Glu Asn Ile Ser Thr Lys Gly Leu
465 470 475 480
Asp Cys Asp Ile Asp Ile Gln Lys Thr Ile Gln Met Val Arg Ala Gln
485 490 495
Arg Ser Gly Met Val Gln Thr Glu Ala Gln Tyr Lys Phe Ile Tyr Val
500 505 510
Ala Ile Ala Gln Phe Ile Glu Thr Thr Lys Lys Lys Leu Glu Val Leu
515 520 525
Gln Ser Gln Lys Gly Gln Glu Ser Glu Tyr Gly Asn Ile Thr Tyr Pro
530 535 540
Pro Ala Met Lys Asn Ala His Ala Lys Ala Ser Arg Thr Ser Ser Lys
545 550 555 560
His Lys Glu Asp Val Tyr Glu Asn Leu His Thr Lys Asn Lys Arg Glu
565 570 575
Glu Lys Val Lys Lys Gln Arg Ser Ala Asp Lys Glu Lys Ser Lys Gly
580 585 590
Ser Leu Lys Arg Lys Arg Ile Leu Gln Ser Thr Val Pro Arg Ala Arg
595 600 605
Asp Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr
610 615 620
Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His
625 630 635 640
Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys
645 650 655
Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp
660 665 670
Pro Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg
675 680 685
Tyr Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro
690 695 700
Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn
705 710 715 720
Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn
725 730 735
Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu
740 745 750
Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met

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        755                 760                 765
Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His
    770                 775                 780
Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn
785                 790                 795                 800
Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu
                805                 810                 815
Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His
            820                 825                 830
Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met
        835                 840                 845
Asp Glu Leu Tyr Lys
    850
```

(2) INFORMATION FOR SEQ ID NO:120:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2994 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...2991
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:120:

```
ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15

GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30

GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45

TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC     192
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60

CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG     240
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80

CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG     288
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95

CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG     336
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Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110

GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC     384
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125

ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC     432
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140

AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC     480
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160

GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC     528
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175

GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC     576
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190

CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG     624
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205

AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC     672
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220

GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC     720
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240

GGA CTC AGA TCT CGA GCT CAA GCT TCG AAT TCG ACC ATG GAG CGG CCC     768
Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Thr Met Glu Arg Pro
                245                 250                 255

CCG GGG CTG CGG CCG GGC GCG GGC GGG CCC TGG GAG ATG CGG GAG CGG     816
Pro Gly Leu Arg Pro Gly Ala Gly Gly Pro Trp Glu Met Arg Glu Arg
            260                 265                 270

CTG GGC ACC GGC GGC TTC GGG AAC GTC TGT CTG TAC CAG CAT CGG GAA     864
Leu Gly Thr Gly Gly Phe Gly Asn Val Cys Leu Tyr Gln His Arg Glu
        275                 280                 285

CTT GAT CTC AAA ATA GCA ATT AAG TCT TGT CGC CTA GAG CTA AGT ACC     912
Leu Asp Leu Lys Ile Ala Ile Lys Ser Cys Arg Leu Glu Leu Ser Thr
    290                 295                 300

AAA AAC AGA GAA CGA TGG TGC CAT GAA ATC CAG ATT ATG AAG AAG TTG     960
Lys Asn Arg Glu Arg Trp Cys His Glu Ile Gln Ile Met Lys Lys Leu
305                 310                 315                 320

AAC CAT GCC AAT GTT GTA AAG GCC TGT GAT GTT CCT GAA GAA TTG AAT    1008
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Asn His Ala Asn Val Val Lys Ala Cys Asp Val Pro Glu Glu Leu Asn
325                 330                 335

ATT TTG ATT CAT GAT GTG CCT CTT CTA GCA ATG GAA TAC TGT TCT GGA    1056
Ile Leu Ile His Asp Val Pro Leu Leu Ala Met Glu Tyr Cys Ser Gly
340                 345                 350

GGA GAT CTC CGA AAG CTG CTC AAC AAA CCA GAA AAT TGT TGT GGA CTT    1104
Gly Asp Leu Arg Lys Leu Leu Asn Lys Pro Glu Asn Cys Cys Gly Leu
355                 360                 365

AAA GAA AGC CAG ATA CTT TCT TTA CTA AGT GAT ATA GGG TCT GGG ATT    1152
Lys Glu Ser Gln Ile Leu Ser Leu Leu Ser Asp Ile Gly Ser Gly Ile
370                 375                 380

CGA TAT TTG CAT GAA AAC AAA ATT ATA CAT CGA GAT CTA AAA CCT GAA    1200
Arg Tyr Leu His Glu Asn Lys Ile Ile His Arg Asp Leu Lys Pro Glu
385                 390                 395                 400

AAC ATA GTT CTT CAG GAT GTT GGT GGA AAG ATA ATA CAT AAA ATA ATT    1248
Asn Ile Val Leu Gln Asp Val Gly Gly Lys Ile Ile His Lys Ile Ile
405                 410                 415

GAT CTG GGA TAT GCC AAA GAT GTT GAT CAA GGA AGT CTG TGT ACA TCT    1296
Asp Leu Gly Tyr Ala Lys Asp Val Asp Gln Gly Ser Leu Cys Thr Ser
420                 425                 430

TTT GTG GGA ACA CTG CAG TAT CTG GCC CCA GAG CTC TTT GAG AAT AAG    1344
Phe Val Gly Thr Leu Gln Tyr Leu Ala Pro Glu Leu Phe Glu Asn Lys
435                 440                 445

CCT TAC ACA GCC ACT GTT GAT TAT TGG AGC TTT GGG ACC ATG GTA TTT    1392
Pro Tyr Thr Ala Thr Val Asp Tyr Trp Ser Phe Gly Thr Met Val Phe
450                 455                 460

GAA TGT ATT GCT GGA TAT AGG CCT TTT TTG CAT CAT CTG CAG CCA TTT    1440
Glu Cys Ile Ala Gly Tyr Arg Pro Phe Leu His His Leu Gln Pro Phe
465                 470                 475                 480

ACC TGG CAT GAG AAG ATT AAG AAG AAG GAT CCA AAG TGT ATA TTT GCA    1488
Thr Trp His Glu Lys Ile Lys Lys Lys Asp Pro Lys Cys Ile Phe Ala
485                 490                 495

TGT GAA GAG ATG TCA GGA GAA GTT CGG TTT AGT AGC CAT TTA CCT CAA    1536
Cys Glu Glu Met Ser Gly Glu Val Arg Phe Ser Ser His Leu Pro Gln
500                 505                 510

CCA AAT AGC CTT TGT AGT TTA ATA GTA GAA CCC ATG GAA AAC TGG CTA    1584
Pro Asn Ser Leu Cys Ser Leu Ile Val Glu Pro Met Glu Asn Trp Leu
515                 520                 525

CAG TTG ATG TTG AAT TGG GAC CCT CAG CAG AGA GGA GGA CCT GTT GAC    1632
Gln Leu Met Leu Asn Trp Asp Pro Gln Gln Arg Gly Gly Pro Val Asp
530                 535                 540

CTT ACT TTG AAG CAG CCA AGA TGT TTT GTA TTA ATG GAT CAC ATT TTG    1680
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Leu Thr Leu Lys Gln Pro Arg Cys Phe Val Leu Met Asp His Ile Leu
545                 550                 555                 560

AAT TTG AAG ATA GTA CAC ATC CTA AAT ATG ACT TCT GCA AAG ATA ATT    1728
Asn Leu Lys Ile Val His Ile Leu Asn Met Thr Ser Ala Lys Ile Ile
                565                 570                 575

TCT TTT CTG TTA CCA CCT GAT GAA AGT CTT CAT TCA CTA CAG TCT CGT    1776
Ser Phe Leu Leu Pro Pro Asp Glu Ser Leu His Ser Leu Gln Ser Arg
            580                 585                 590

ATT GAG CGT GAA ACT GGA ATA AAT ACT GGT TCT CAA GAA CTT CTT TCA    1824
Ile Glu Arg Glu Thr Gly Ile Asn Thr Gly Ser Gln Glu Leu Leu Ser
        595                 600                 605

GAG ACA GGA ATT TCT CTG GAT CCT CGG AAA CCA GCC TCT CAA TGT GTT    1872
Glu Thr Gly Ile Ser Leu Asp Pro Arg Lys Pro Ala Ser Gln Cys Val
    610                 615                 620

CTA GAT GGA GTT AGA GGC TGT GAT AGC TAT ATG GTT TAT TTG TTT GAT    1920
Leu Asp Gly Val Arg Gly Cys Asp Ser Tyr Met Val Tyr Leu Phe Asp
625                 630                 635                 640

AAA AGT AAA ACT GTA TAT GAA GGG CCA TTT GCT TCC AGA AGT TTA TCT    1968
Lys Ser Lys Thr Val Tyr Glu Gly Pro Phe Ala Ser Arg Ser Leu Ser
                645                 650                 655

GAT TGT GTA AAT TAT ATT GTA CAG GAC AGC AAA ATA CAG CTT CCA ATT    2016
Asp Cys Val Asn Tyr Ile Val Gln Asp Ser Lys Ile Gln Leu Pro Ile
            660                 665                 670

ATA CAG CTG CGT AAA GTG TGG GCT GAA GCA GTG CAC TAT GTG TCT GGA    2064
Ile Gln Leu Arg Lys Val Trp Ala Glu Ala Val His Tyr Val Ser Gly
        675                 680                 685

CTA AAA GAA GAC TAT AGC AGG CTC TTT CAG GGA CAA AGG GCA GCA ATG    2112
Leu Lys Glu Asp Tyr Ser Arg Leu Phe Gln Gly Gln Arg Ala Ala Met
    690                 695                 700

TTA AGT CTT CTT AGA TAT AAT GCT AAC TTA ACA AAA ATG AAG AAC ACT    2160
Leu Ser Leu Leu Arg Tyr Asn Ala Asn Leu Thr Lys Met Lys Asn Thr
705                 710                 715                 720

TTG ATC TCA GCA TCA CAA CAA CTG AAA GCT AAA TTG GAG TTT TTT CAC    2208
Leu Ile Ser Ala Ser Gln Gln Leu Lys Ala Lys Leu Glu Phe Phe His
                725                 730                 735

AAA AGC ATT CAG CTT GAC TTG GAG AGA TAC AGC GAG CAG ATG ACG TAT    2256
Lys Ser Ile Gln Leu Asp Leu Glu Arg Tyr Ser Glu Gln Met Thr Tyr
            740                 745                 750

GGG ATA TCT TCA GAA AAA ATG CTA AAA GCA TGG AAA GAA ATG GAA GAA    2304
Gly Ile Ser Ser Glu Lys Met Leu Lys Ala Trp Lys Glu Met Glu Glu
        755                 760                 765

AAG GCC ATC CAC TAT GCT GAG GTT GGT GTC ATT GGA TAC CTG GAG GAT    2352
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Lys Ala Ile His Tyr Ala Glu Val Gly Val Ile Gly Tyr Leu Glu Asp
    770                 775                 780

CAG ATT ATG TCT TTG CAT GCT GAA ATC ATG GGG CTA CAG AAG AGC CCC    2400
Gln Ile Met Ser Leu His Ala Glu Ile Met Gly Leu Gln Lys Ser Pro
785                 790                 795                 800

TAT GGA AGA CGT CAG GGA GAC TTG ATG GAA TCT CTG GAA CAG CGT GCC    2448
Tyr Gly Arg Arg Gln Gly Asp Leu Met Glu Ser Leu Glu Gln Arg Ala
                805                 810                 815

ATT GAT CTA TAT AAG CAG TTA AAA CAC AGA CCT TCA GAT CAC TCC TAC    2496
Ile Asp Leu Tyr Lys Gln Leu Lys His Arg Pro Ser Asp His Ser Tyr
            820                 825                 830

AGT GAC AGC ACA GAG ATG GTG AAA ATC ATT GTG CAC ACT GTG CAG AGT    2544
Ser Asp Ser Thr Glu Met Val Lys Ile Ile Val His Thr Val Gln Ser
        835                 840                 845

CAG GAC CGT GTG CTC AAG GAG CTG TTT GGT CAT TTG AGC AAG TTG TTG    2592
Gln Asp Arg Val Leu Lys Glu Leu Phe Gly His Leu Ser Lys Leu Leu
    850                 855                 860

GGC TGT AAG CAG AAG ATT ATT GAT CTA CTC CCT AAG GTG GAA GTG GCC    2640
Gly Cys Lys Gln Lys Ile Ile Asp Leu Leu Pro Lys Val Glu Val Ala
865                 870                 875                 880

CTC AGT AAT ATC AAA GAA GCT GAC AAT ACT GTC ATG TTC ATG CAG GGA    2688
Leu Ser Asn Ile Lys Glu Ala Asp Asn Thr Val Met Phe Met Gln Gly
                885                 890                 895

AAA AGG CAG AAA GAA ATA TGG CAT CTC CTT AAA ATT GCC TGT ACA CAG    2736
Lys Arg Gln Lys Glu Ile Trp His Leu Leu Lys Ile Ala Cys Thr Gln
            900                 905                 910

AGT TCT GCC CGC TCT CTT GTA GGA TCC AGT CTA GAA GGT GCA GTA ACC    2784
Ser Ser Ala Arg Ser Leu Val Gly Ser Ser Leu Glu Gly Ala Val Thr
        915                 920                 925

CCT CAG ACA TCA GCA TGG CTG CCC CCG ACT TCA GCA GAA CAT GAT CAT    2832
Pro Gln Thr Ser Ala Trp Leu Pro Pro Thr Ser Ala Glu His Asp His
    930                 935                 940

TCT CTG TCA TGT GTG GTA ACT CCT CAA GAT GGG GAG ACT TCA GCA CAA    2880
Ser Leu Ser Cys Val Val Thr Pro Gln Asp Gly Glu Thr Ser Ala Gln
945                 950                 955                 960

ATG ATA GAA GAA AAT TTG AAC TGC CTT GGC CAT TTA AGC ACT ATT ATT    2928
Met Ile Glu Glu Asn Leu Asn Cys Leu Gly His Leu Ser Thr Ile Ile
                965                 970                 975

CAT GAG GCA AAT GAG GAA CAG GGC AAT AGT ATG ATG AAT CTT GAT TGG    2976
His Glu Ala Asn Glu Glu Gln Gly Asn Ser Met Met Asn Leu Asp Trp
            980                 985                 990

AGT TGG TTA ACA GAA TGA                                            2994
```

Ser Trp Leu Thr Glu
995

(2) INFORMATION FOR SEQ ID NO:121:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 997 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:121:

```
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240
Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Thr Met Glu Arg Pro
                245                 250                 255
Pro Gly Leu Arg Pro Gly Ala Gly Gly Pro Trp Glu Met Arg Glu Arg
            260                 265                 270
Leu Gly Thr Gly Gly Phe Gly Asn Val Cys Leu Tyr Gln His Arg Glu
        275                 280                 285
Leu Asp Leu Lys Ile Ala Ile Lys Ser Cys Arg Leu Glu Leu Ser Thr
    290                 295                 300
Lys Asn Arg Glu Arg Trp Cys His Glu Ile Gln Ile Met Lys Lys Leu
```

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305                 310                 315                 320
Asn His Ala Asn Val Val Lys Ala Cys Asp Val Pro Glu Glu Leu Asn
                325                 330                 335
Ile Leu Ile His Asp Val Pro Leu Leu Ala Met Glu Tyr Cys Ser Gly
            340                 345                 350
Gly Asp Leu Arg Lys Leu Leu Asn Lys Pro Glu Asn Cys Cys Gly Leu
        355                 360                 365
Lys Glu Ser Gln Ile Leu Ser Leu Leu Ser Asp Ile Gly Ser Gly Ile
    370                 375                 380
Arg Tyr Leu His Glu Asn Lys Ile Ile His Arg Asp Leu Lys Pro Glu
385                 390                 395                 400
Asn Ile Val Leu Gln Asp Val Gly Gly Lys Ile Ile His Lys Ile Ile
                405                 410                 415
Asp Leu Gly Tyr Ala Lys Asp Val Asp Gln Gly Ser Leu Cys Thr Ser
            420                 425                 430
Phe Val Gly Thr Leu Gln Tyr Leu Ala Pro Glu Leu Phe Glu Asn Lys
        435                 440                 445
Pro Tyr Thr Ala Thr Val Asp Tyr Trp Ser Phe Gly Thr Met Val Phe
    450                 455                 460
Glu Cys Ile Ala Gly Tyr Arg Pro Phe Leu His His Leu Gln Pro Phe
465                 470                 475                 480
Thr Trp His Glu Lys Ile Lys Lys Lys Asp Pro Lys Cys Ile Phe Ala
                485                 490                 495
Cys Glu Glu Met Ser Gly Glu Val Arg Phe Ser Ser His Leu Pro Gln
            500                 505                 510
Pro Asn Ser Leu Cys Ser Leu Ile Val Glu Pro Met Glu Asn Trp Leu
        515                 520                 525
Gln Leu Met Leu Asn Trp Asp Pro Gln Gln Arg Gly Gly Pro Val Asp
    530                 535                 540
Leu Thr Leu Lys Gln Pro Arg Cys Phe Val Leu Met Asp His Ile Leu
545                 550                 555                 560
Asn Leu Lys Ile Val His Ile Leu Asn Met Thr Ser Ala Lys Ile Ile
                565                 570                 575
Ser Phe Leu Leu Pro Pro Asp Glu Ser Leu His Ser Leu Gln Ser Arg
            580                 585                 590
Ile Glu Arg Glu Thr Gly Ile Asn Thr Gly Ser Gln Glu Leu Leu Ser
        595                 600                 605
Glu Thr Gly Ile Ser Leu Asp Pro Arg Lys Pro Ala Ser Gln Cys Val
    610                 615                 620
Leu Asp Gly Val Arg Gly Cys Asp Ser Tyr Met Val Tyr Leu Phe Asp
625                 630                 635                 640
Lys Ser Lys Thr Val Tyr Glu Gly Pro Phe Ala Ser Arg Ser Leu Ser
                645                 650                 655
Asp Cys Val Asn Tyr Ile Val Gln Asp Ser Lys Ile Gln Leu Pro Ile
            660                 665                 670
Ile Gln Leu Arg Lys Val Trp Ala Glu Ala Val His Tyr Val Ser Gly
        675                 680                 685
Leu Lys Glu Asp Tyr Ser Arg Leu Phe Gln Gly Gln Arg Ala Ala Met
    690                 695                 700
Leu Ser Leu Leu Arg Tyr Asn Ala Asn Leu Thr Lys Met Lys Asn Thr
705                 710                 715                 720
Leu Ile Ser Ala Ser Gln Gln Leu Lys Ala Lys Leu Glu Phe Phe His
                725                 730                 735
Lys Ser Ile Gln Leu Asp Leu Glu Arg Tyr Ser Glu Gln Met Thr Tyr
            740                 745                 750
Gly Ile Ser Ser Glu Lys Met Leu Lys Ala Trp Lys Glu Met Glu Glu
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          755                 760                 765
Lys Ala Ile His Tyr Ala Glu Val Gly Val Ile Gly Tyr Leu Glu Asp
    770                 775                 780
Gln Ile Met Ser Leu His Ala Glu Ile Met Gly Leu Gln Lys Ser Pro
785                 790                 795                 800
Tyr Gly Arg Arg Gln Gly Asp Leu Met Glu Ser Leu Glu Gln Arg Ala
                805                 810                 815
Ile Asp Leu Tyr Lys Gln Leu Lys His Arg Pro Ser Asp His Ser Tyr
            820                 825                 830
Ser Asp Ser Thr Glu Met Val Lys Ile Ile Val His Thr Val Gln Ser
          835                 840                 845
Gln Asp Arg Val Leu Lys Glu Leu Phe Gly His Leu Ser Lys Leu Leu
    850                 855                 860
Gly Cys Lys Gln Lys Ile Ile Asp Leu Leu Pro Lys Val Glu Val Ala
865                 870                 875                 880
Leu Ser Asn Ile Lys Glu Ala Asp Asn Thr Val Met Phe Met Gln Gly
                885                 890                 895
Lys Arg Gln Lys Glu Ile Trp His Leu Leu Lys Ile Ala Cys Thr Gln
            900                 905                 910
Ser Ser Ala Arg Ser Leu Val Gly Ser Ser Leu Glu Gly Ala Val Thr
          915                 920                 925
Pro Gln Thr Ser Ala Trp Leu Pro Pro Thr Ser Ala Glu His Asp His
    930                 935                 940
Ser Leu Ser Cys Val Val Thr Pro Gln Asp Gly Glu Thr Ser Ala Gln
945                 950                 955                 960
Met Ile Glu Glu Asn Leu Asn Cys Leu Gly His Leu Ser Thr Ile Ile
                965                 970                 975
His Glu Ala Asn Glu Glu Gln Gly Asn Ser Met Met Asn Leu Asp Trp
            980                 985                 990
Ser Trp Leu Thr Glu
          995
```

(2) INFORMATION FOR SEQ ID NO:122:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2991 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...2988
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:122:

```
ATG GAG CGG CCC CCG GGG CTG CGG CCG GGC GCG GGC GGG CCC TGG GAG      48
Met Glu Arg Pro Pro Gly Leu Arg Pro Gly Ala Gly Gly Pro Trp Glu
 1               5                  10                  15

ATG CGG GAG CGG CTG GGC ACC GGC GGC TTC GGG AAC GTC TGT CTG TAC      96
Met Arg Glu Arg Leu Gly Thr Gly Gly Phe Gly Asn Val Cys Leu Tyr
            20                  25                  30
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CAG CAT CGG GAA CTT GAT CTC AAA ATA GCA ATT AAG TCT TGT CGC CTA      144
Gln His Arg Glu Leu Asp Leu Lys Ile Ala Ile Lys Ser Cys Arg Leu
        35                  40                  45

GAG CTA AGT ACC AAA AAC AGA GAA CGA TGG TGC CAT GAA ATC CAG ATT      192
Glu Leu Ser Thr Lys Asn Arg Glu Arg Trp Cys His Glu Ile Gln Ile
    50                  55                  60

ATG AAG AAG TTG AAC CAT GCC AAT GTT GTA AAG GCC TGT GAT GTT CCT      240
Met Lys Lys Leu Asn His Ala Asn Val Val Lys Ala Cys Asp Val Pro
65                  70                  75                  80

GAA GAA TTG AAT ATT TTG ATT CAT GAT GTG CCT CTT CTA GCA ATG GAA      288
Glu Glu Leu Asn Ile Leu Ile His Asp Val Pro Leu Leu Ala Met Glu
                85                  90                  95

TAC TGT TCT GGA GGA GAT CTC CGA AAG CTG CTC AAC AAA CCA GAA AAT      336
Tyr Cys Ser Gly Gly Asp Leu Arg Lys Leu Leu Asn Lys Pro Glu Asn
            100                 105                 110

TGT TGT GGA CTT AAA GAA AGC CAG ATA CTT TCT TTA CTA AGT GAT ATA      384
Cys Cys Gly Leu Lys Glu Ser Gln Ile Leu Ser Leu Leu Ser Asp Ile
        115                 120                 125

GGG TCT GGG ATT CGA TAT TTG CAT GAA AAC AAA ATT ATA CAT CGA GAT      432
Gly Ser Gly Ile Arg Tyr Leu His Glu Asn Lys Ile Ile His Arg Asp
    130                 135                 140

CTA AAA CCT GAA AAC ATA GTT CTT CAG GAT GTT GGT GGA AAG ATA ATA      480
Leu Lys Pro Glu Asn Ile Val Leu Gln Asp Val Gly Gly Lys Ile Ile
145                 150                 155                 160

CAT AAA ATA ATT GAT CTG GGA TAT GCC AAA GAT GTT GAT CAA GGA AGT      528
His Lys Ile Ile Asp Leu Gly Tyr Ala Lys Asp Val Asp Gln Gly Ser
                165                 170                 175

CTG TGT ACA TCT TTT GTG GGA ACA CTG CAG TAT CTG GCC CCA GAG CTC      576
Leu Cys Thr Ser Phe Val Gly Thr Leu Gln Tyr Leu Ala Pro Glu Leu
            180                 185                 190

TTT GAG AAT AAG CCT TAC ACA GCC ACT GTT GAT TAT TGG AGC TTT GGG      624
Phe Glu Asn Lys Pro Tyr Thr Ala Thr Val Asp Tyr Trp Ser Phe Gly
        195                 200                 205

ACC ATG GTA TTT GAA TGT ATT GCT GGA TAT AGG CCT TTT TTG CAT CAT      672
Thr Met Val Phe Glu Cys Ile Ala Gly Tyr Arg Pro Phe Leu His His
    210                 215                 220

CTG CAG CCA TTT ACC TGG CAT GAG AAG ATT AAG AAG AAG GAT CCA AAG      720
Leu Gln Pro Phe Thr Trp His Glu Lys Ile Lys Lys Lys Asp Pro Lys
225                 230                 235                 240

TGT ATA TTT GCA TGT GAA GAG ATG TCA GGA GAA GTT CGG TTT AGT AGC      768
Cys Ile Phe Ala Cys Glu Glu Met Ser Gly Glu Val Arg Phe Ser Ser
                245                 250                 255
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CAT TTA CCT CAA CCA AAT AGC CTT TGT AGT TTA ATA GTA GAA CCC ATG      816
His Leu Pro Gln Pro Asn Ser Leu Cys Ser Leu Ile Val Glu Pro Met
            260                 265                 270

GAA AAC TGG CTA CAG TTG ATG TTG AAT TGG GAC CCT CAG CAG AGA GGA      864
Glu Asn Trp Leu Gln Leu Met Leu Asn Trp Asp Pro Gln Gln Arg Gly
        275                 280                 285

GGA CCT GTT GAC CTT ACT TTG AAG CAG CCA AGA TGT TTT GTA TTA ATG      912
Gly Pro Val Asp Leu Thr Leu Lys Gln Pro Arg Cys Phe Val Leu Met
    290                 295                 300

GAT CAC ATT TTG AAT TTG AAG ATA GTA CAC ATC CTA AAT ATG ACT TCT      960
Asp His Ile Leu Asn Leu Lys Ile Val His Ile Leu Asn Met Thr Ser
305                 310                 315                 320

GCA AAG ATA ATT TCT TTT CTG TTA CCA CCT GAT GAA AGT CTT CAT TCA     1008
Ala Lys Ile Ile Ser Phe Leu Leu Pro Pro Asp Glu Ser Leu His Ser
                325                 330                 335

CTA CAG TCT CGT ATT GAG CGT GAA ACT GGA ATA AAT ACT GGT TCT CAA     1056
Leu Gln Ser Arg Ile Glu Arg Glu Thr Gly Ile Asn Thr Gly Ser Gln
            340                 345                 350

GAA CTT CTT TCA GAG ACA GGA ATT TCT CTG GAT CCT CGG AAA CCA GCC     1104
Glu Leu Leu Ser Glu Thr Gly Ile Ser Leu Asp Pro Arg Lys Pro Ala
        355                 360                 365

TCT CAA TGT GTT CTA GAT GGA GTT AGA GGC TGT GAT AGC TAT ATG GTT     1152
Ser Gln Cys Val Leu Asp Gly Val Arg Gly Cys Asp Ser Tyr Met Val
    370                 375                 380

TAT TTG TTT GAT AAA AGT AAA ACT GTA TAT GAA GGG CCA TTT GCT TCC     1200
Tyr Leu Phe Asp Lys Ser Lys Thr Val Tyr Glu Gly Pro Phe Ala Ser
385                 390                 395                 400

AGA AGT TTA TCT GAT TGT GTA AAT TAT ATT GTA CAG GAC AGC AAA ATA     1248
Arg Ser Leu Ser Asp Cys Val Asn Tyr Ile Val Gln Asp Ser Lys Ile
                405                 410                 415

CAG CTT CCA ATT ATA CAG CTG CGT AAA GTG TGG GCT GAA GCA GTG CAC     1296
Gln Leu Pro Ile Ile Gln Leu Arg Lys Val Trp Ala Glu Ala Val His
            420                 425                 430

TAT GTG TCT GGA CTA AAA GAA GAC TAT AGC AGG CTC TTT CAG GGA CAA     1344
Tyr Val Ser Gly Leu Lys Glu Asp Tyr Ser Arg Leu Phe Gln Gly Gln
        435                 440                 445

AGG GCA GCA ATG TTA AGT CTT CTT AGA TAT AAT GCT AAC TTA ACA AAA     1392
Arg Ala Ala Met Leu Ser Leu Leu Arg Tyr Asn Ala Asn Leu Thr Lys
    450                 455                 460

ATG AAG AAC ACT TTG ATC TCA GCA TCA CAA CAA CTG AAA GCT AAA TTG     1440
Met Lys Asn Thr Leu Ile Ser Ala Ser Gln Gln Leu Lys Ala Lys Leu
465                 470                 475                 480
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BNSDOCID: <WO___9845704A2_I_>

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GAG TTT TTT CAC AAA AGC ATT CAG CTT GAC TTG GAG AGA TAC AGC GAG    1488
Glu Phe Phe His Lys Ser Ile Gln Leu Asp Leu Glu Arg Tyr Ser Glu
                485                 490                 495

CAG ATG ACG TAT GGG ATA TCT TCA GAA AAA ATG CTA AAA GCA TGG AAA    1536
Gln Met Thr Tyr Gly Ile Ser Ser Glu Lys Met Leu Lys Ala Trp Lys
            500                 505                 510

GAA ATG GAA GAA AAG GCC ATC CAC TAT GCT GAG GTT GGT GTC ATT GGA    1584
Glu Met Glu Glu Lys Ala Ile His Tyr Ala Glu Val Gly Val Ile Gly
        515                 520                 525

TAC CTG GAG GAT CAG ATT ATG TCT TTG CAT GCT GAA ATC ATG GGG CTA    1632
Tyr Leu Glu Asp Gln Ile Met Ser Leu His Ala Glu Ile Met Gly Leu
    530                 535                 540

CAG AAG AGC CCC TAT GGA AGA CGT CAG GGA GAC TTG ATG GAA TCT CTG    1680
Gln Lys Ser Pro Tyr Gly Arg Arg Gln Gly Asp Leu Met Glu Ser Leu
545                 550                 555                 560

GAA CAG CGT GCC ATT GAT CTA TAT AAG CAG TTA AAA CAC AGA CCT TCA    1728
Glu Gln Arg Ala Ile Asp Leu Tyr Lys Gln Leu Lys His Arg Pro Ser
                565                 570                 575

GAT CAC TCC TAC AGT GAC AGC ACA GAG ATG GTG AAA ATC ATT GTG CAC    1776
Asp His Ser Tyr Ser Asp Ser Thr Glu Met Val Lys Ile Ile Val His
            580                 585                 590

ACT GTG CAG AGT CAG GAC CGT GTG CTC AAG GAG CTG TTT GGT CAT TTG    1824
Thr Val Gln Ser Gln Asp Arg Val Leu Lys Glu Leu Phe Gly His Leu
        595                 600                 605

AGC AAG TTG TTG GGC TGT AAG CAG AAG ATT ATT GAT CTA CTC CCT AAG    1872
Ser Lys Leu Leu Gly Cys Lys Gln Lys Ile Ile Asp Leu Leu Pro Lys
    610                 615                 620

GTG GAA GTG GCC CTC AGT AAT ATC AAA GAA GCT GAC AAT ACT GTC ATG    1920
Val Glu Val Ala Leu Ser Asn Ile Lys Glu Ala Asp Asn Thr Val Met
625                 630                 635                 640

TTC ATG CAG GGA AAA AGG CAG AAA GAA ATA TGG CAT CTC CTT AAA ATT    1968
Phe Met Gln Gly Lys Arg Gln Lys Glu Ile Trp His Leu Leu Lys Ile
                645                 650                 655

GCC TGT ACA CAG AGT TCT GCC CGC TCT CTT GTA GGA TCC AGT CTA GAA    2016
Ala Cys Thr Gln Ser Ser Ala Arg Ser Leu Val Gly Ser Ser Leu Glu
            660                 665                 670

GGT GCA GTA ACC CCT CAG ACA TCA GCA TGG CTG CCC CCG ACT TCA GCA    2064
Gly Ala Val Thr Pro Gln Thr Ser Ala Trp Leu Pro Pro Thr Ser Ala
        675                 680                 685

GAA CAT GAT CAT TCT CTG TCA TGT GTG GTA ACT CCT CAA GAT GGG GAG    2112
Glu His Asp His Ser Leu Ser Cys Val Val Thr Pro Gln Asp Gly Glu
    690                 695                 700
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ACT TCA GCA CAA ATG ATA GAA GAA AAT TTG AAC TGC CTT GGC CAT TTA    2160
Thr Ser Ala Gln Met Ile Glu Glu Asn Leu Asn Cys Leu Gly His Leu
705                 710                 715                 720

AGC ACT ATT ATT CAT GAG GCA AAT GAG GAA CAG GGC AAT AGT ATG ATG    2208
Ser Thr Ile Ile His Glu Ala Asn Glu Glu Gln Gly Asn Ser Met Met
                725                 730                 735

AAT CTT GAT TGG AGT TGG TTA ACA GAA TGG GTA CCG CGG GCC CGG GAT    2256
Asn Leu Asp Trp Ser Trp Leu Thr Glu Trp Val Pro Arg Ala Arg Asp
            740                 745                 750

CCA CCG GTC GCC ACC ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG    2304
Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly
        755                 760                 765

GTG GTG CCC ATC CTG GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG    2352
Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys
    770                 775                 780

TTC AGC GTG TCC GGC GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG    2400
Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu
785                 790                 795                 800

ACC CTG AAG TTC ATC TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC    2448
Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro
                805                 810                 815

ACC CTC GTG ACC ACC CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC    2496
Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr
            820                 825                 830

CCC GAC CAC ATG AAG CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA    2544
Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu
        835                 840                 845

GGC TAC GTC CAG GAG CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC    2592
Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr
    850                 855                 860

AAG ACC CGC GCC GAG GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC    2640
Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg
865                 870                 875                 880

ATC GAG CTG AAG GGC ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG    2688
Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly
                885                 890                 895

CAC AAG CTG GAG TAC AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC    2736
His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala
            900                 905                 910

GAC AAG CAG AAG AAC GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC    2784
Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn
        915                 920                 925
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ATC GAG GAC GGC AGC GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC     2832
Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr
    930                 935                 940

CCC ATC GGC GAC GGC CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC     2880
Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser
945                 950                 955                 960

ACC CAG TCC GCC CTG AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG     2928
Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met
                965                 970                 975

GTC CTG CTG GAG TTC GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC     2976
Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp
            980                 985                 990

GAG CTG TAC AAG TAA                                                 2991
Glu Leu Tyr Lys
        995
```

(2) INFORMATION FOR SEQ ID NO:123:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 996 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:123:

```
Met Glu Arg Pro Pro Gly Leu Arg Pro Gly Ala Gly Gly Pro Trp Glu
 1               5                  10                  15
Met Arg Glu Arg Leu Gly Thr Gly Gly Phe Gly Asn Val Cys Leu Tyr
            20                  25                  30
Gln His Arg Glu Leu Asp Leu Lys Ile Ala Ile Lys Ser Cys Arg Leu
        35                  40                  45
Glu Leu Ser Thr Lys Asn Arg Glu Arg Trp Cys His Glu Ile Gln Ile
    50                  55                  60
Met Lys Lys Leu Asn His Ala Asn Val Val Lys Ala Cys Asp Val Pro
65                  70                  75                  80
Glu Glu Leu Asn Ile Leu Ile His Asp Val Pro Leu Leu Ala Met Glu
                85                  90                  95
Tyr Cys Ser Gly Gly Asp Leu Arg Lys Leu Leu Asn Lys Pro Glu Asn
            100                 105                 110
Cys Cys Gly Leu Lys Glu Ser Gln Ile Leu Ser Leu Leu Ser Asp Ile
        115                 120                 125
Gly Ser Gly Ile Arg Tyr Leu His Glu Asn Lys Ile Ile His Arg Asp
    130                 135                 140
Leu Lys Pro Glu Asn Ile Val Leu Gln Asp Val Gly Gly Lys Ile Ile
145                 150                 155                 160
His Lys Ile Ile Asp Leu Gly Tyr Ala Lys Asp Val Asp Gln Gly Ser
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                    165                 170                 175
Leu Cys Thr Ser Phe Val Gly Thr Leu Gln Tyr Leu Ala Pro Glu Leu
                180                 185                 190
Phe Glu Asn Lys Pro Tyr Thr Ala Thr Val Asp Tyr Trp Ser Phe Gly
        195                 200                 205
Thr Met Val Phe Glu Cys Ile Ala Gly Tyr Arg Pro Phe Leu His His
    210                 215                 220
Leu Gln Pro Phe Thr Trp His Glu Lys Ile Lys Lys Lys Asp Pro Lys
225                 230                 235                 240
Cys Ile Phe Ala Cys Glu Glu Met Ser Gly Glu Val Arg Phe Ser Ser
                245                 250                 255
His Leu Pro Gln Pro Asn Ser Leu Cys Ser Leu Ile Val Glu Pro Met
            260                 265                 270
Glu Asn Trp Leu Gln Leu Met Leu Asn Trp Asp Pro Gln Gln Arg Gly
        275                 280                 285
Gly Pro Val Asp Leu Thr Leu Lys Gln Pro Arg Cys Phe Val Leu Met
    290                 295                 300
Asp His Ile Leu Asn Leu Lys Ile Val His Ile Leu Asn Met Thr Ser
305                 310                 315                 320
Ala Lys Ile Ile Ser Phe Leu Leu Pro Pro Asp Glu Ser Leu His Ser
                325                 330                 335
Leu Gln Ser Arg Ile Glu Arg Glu Thr Gly Ile Asn Thr Gly Ser Gln
            340                 345                 350
Glu Leu Leu Ser Glu Thr Gly Ile Ser Leu Asp Pro Arg Lys Pro Ala
        355                 360                 365
Ser Gln Cys Val Leu Asp Gly Val Arg Gly Cys Asp Ser Tyr Met Val
    370                 375                 380
Tyr Leu Phe Asp Lys Ser Lys Thr Val Tyr Glu Gly Pro Phe Ala Ser
385                 390                 395                 400
Arg Ser Leu Ser Asp Cys Val Asn Tyr Ile Val Gln Asp Ser Lys Ile
                405                 410                 415
Gln Leu Pro Ile Ile Gln Leu Arg Lys Val Trp Ala Glu Ala Val His
            420                 425                 430
Tyr Val Ser Gly Leu Lys Glu Asp Tyr Ser Arg Leu Phe Gln Gly Gln
        435                 440                 445
Arg Ala Ala Met Leu Ser Leu Leu Arg Tyr Asn Ala Asn Leu Thr Lys
    450                 455                 460
Met Lys Asn Thr Leu Ile Ser Ala Ser Gln Gln Leu Lys Ala Lys Leu
465                 470                 475                 480
Glu Phe Phe His Lys Ser Ile Gln Leu Asp Leu Glu Arg Tyr Ser Glu
                485                 490                 495
Gln Met Thr Tyr Gly Ile Ser Ser Glu Lys Met Leu Lys Ala Trp Lys
            500                 505                 510
Glu Met Glu Glu Lys Ala Ile His Tyr Ala Glu Val Gly Val Ile Gly
        515                 520                 525
Tyr Leu Glu Asp Gln Ile Met Ser Leu His Ala Glu Ile Met Gly Leu
    530                 535                 540
Gln Lys Ser Pro Tyr Gly Arg Arg Gln Gly Asp Leu Met Glu Ser Leu
545                 550                 555                 560
Glu Gln Arg Ala Ile Asp Leu Tyr Lys Gln Leu Lys His Arg Pro Ser
                565                 570                 575
Asp His Ser Tyr Ser Asp Ser Thr Glu Met Val Lys Ile Ile Val His
            580                 585                 590
Thr Val Gln Ser Gln Asp Arg Val Leu Lys Glu Leu Phe Gly His Leu
        595                 600                 605
Ser Lys Leu Leu Gly Cys Lys Gln Lys Ile Ile Asp Leu Leu Pro Lys
```

240

610 615 620
Val Glu Val Ala Leu Ser Asn Ile Lys Glu Ala Asp Asn Thr Val Met
625 630 635 640
Phe Met Gln Gly Lys Arg Gln Lys Glu Ile Trp His Leu Leu Lys Ile
645 650 655
Ala Cys Thr Gln Ser Ser Ala Arg Ser Leu Val Gly Ser Ser Leu Glu
660 665 670
Gly Ala Val Thr Pro Gln Thr Ser Ala Trp Leu Pro Pro Thr Ser Ala
675 680 685
Glu His Asp His Ser Leu Ser Cys Val Val Thr Pro Gln Asp Gly Glu
690 695 700
Thr Ser Ala Gln Met Ile Glu Glu Asn Leu Asn Cys Leu Gly His Leu
705 710 715 720
Ser Thr Ile Ile His Glu Ala Asn Glu Glu Gln Gly Asn Ser Met Met
725 730 735
Asn Leu Asp Trp Ser Trp Leu Thr Glu Trp Val Pro Arg Ala Arg Asp
740 745 750
Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly
755 760 765
Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys
770 775 780
Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu
785 790 795 800
Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro
805 810 815
Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr
820 825 830
Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu
835 840 845
Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr
850 855 860
Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg
865 870 875 880
Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly
885 890 895
His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala
900 905 910
Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn
915 920 925
Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr
930 935 940
Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser
945 950 955 960
Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met
965 970 975
Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp
980 985 990
Glu Leu Tyr Lys
995

(2) INFORMATION FOR SEQ ID NO:124:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1908 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single

240

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...1905
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:124:

```
ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15

GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30

GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45

TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC     192
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60

CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG     240
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80

CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG     288
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95

CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG     336
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110

GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC     384
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125

ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC     432
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140

AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC     480
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160

GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC     528
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175

GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC     576
```

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Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190

CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG     624
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205

AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC     672
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220

GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC     720
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240

GGA CTC AGA TCT CGA GCT CAA GCT TCC ATG AGC GAG ACG GTC ATC ATG     768
Gly Leu Arg Ser Arg Ala Gln Ala Ser Met Ser Glu Thr Val Ile Met
                245                 250                 255

AGC GAG ACG GTC ATC TGT TCC AGC CGG GCC ACT GTG ATG CTT TAT GAT     816
Ser Glu Thr Val Ile Cys Ser Ser Arg Ala Thr Val Met Leu Tyr Asp
            260                 265                 270

GAT GGC AAC AAG CGA TGG CTC CCT GCT GGC ACG GGT CCC CAG GCC TTC     864
Asp Gly Asn Lys Arg Trp Leu Pro Ala Gly Thr Gly Pro Gln Ala Phe
        275                 280                 285

AGC CGC GTC CAG ATC TAC CAC AAC CCC ACG GCC AAT TCC TTT CGC GTC     912
Ser Arg Val Gln Ile Tyr His Asn Pro Thr Ala Asn Ser Phe Arg Val
    290                 295                 300

GTG GGC CGG AAG ATG CAG CCC GAC CAG CAG GTG GTC ATC AAC TGT GCC     960
Val Gly Arg Lys Met Gln Pro Asp Gln Gln Val Val Ile Asn Cys Ala
305                 310                 315                 320

ATC GTC CGG GGT GTC AAG TAT AAC CAG GCC ACC CCC AAC TTC CAT CAG    1008
Ile Val Arg Gly Val Lys Tyr Asn Gln Ala Thr Pro Asn Phe His Gln
                325                 330                 335

TGG CGC GAC GCT CGC CAG GTC TGG GGC CTC AAC TTC GGC AGC AAG GAG    1056
Trp Arg Asp Ala Arg Gln Val Trp Gly Leu Asn Phe Gly Ser Lys Glu
            340                 345                 350

GAT GCG GCC CAG TTT GCC GCC GGC ATG GCC AGT GCC CTA GAG GCG TTG    1104
Asp Ala Ala Gln Phe Ala Ala Gly Met Ala Ser Ala Leu Glu Ala Leu
        355                 360                 365

GAA GGA GGT GGG CCC CCT CCA CCC CCA GCA CTT CCC ACC TGG TCG GTC    1152
Glu Gly Gly Gly Pro Pro Pro Pro Pro Ala Leu Pro Thr Trp Ser Val
    370                 375                 380

CCG AAC GGC CCC TCC CCG GAG GAG GTG GAG CAG CAG AAA AGG CAG CAG    1200
Pro Asn Gly Pro Ser Pro Glu Glu Val Glu Gln Gln Lys Arg Gln Gln
385                 390                 395                 400

CCC GGC CCG TCG GAG CAC ATA GAG CGC CGG GTC TCC AAT GCA GGA GGC    1248
```

```
Pro Gly Pro Ser Glu His Ile Glu Arg Arg Val Ser Asn Ala Gly Gly
                405                 410                 415

CCA CCT GCT CCC CCC GCT GGG GGT CCA CCC CCA CCA CCA GGA CCT CCC    1296
Pro Pro Ala Pro Pro Ala Gly Gly Pro Pro Pro Pro Pro Gly Pro Pro
            420                 425                 430

CCT CCT CCA GGT CCC CCC CCA CCC CCA GGT TTG CCC CCT TCG GGG GTC    1344
Pro Pro Pro Gly Pro Pro Pro Pro Pro Gly Leu Pro Pro Ser Gly Val
        435                 440                 445

CCA GCT GCA GCG CAC GGA GCA GGG GGA GGA CCA CCC CCT GCA CCC CCT    1392
Pro Ala Ala Ala His Gly Ala Gly Gly Gly Pro Pro Pro Ala Pro Pro
    450                 455                 460

CTC CCG GCA GCA CAG GGC CCT GGT GGT GGG GGA GCT GGG GCC CCA GGC    1440
Leu Pro Ala Ala Gln Gly Pro Gly Gly Gly Gly Ala Gly Ala Pro Gly
465                 470                 475                 480

CTG GCC GCA GCT ATT GCT GGA GCC AAA CTC AGG AAA GTC AGC AAG CAG    1488
Leu Ala Ala Ala Ile Ala Gly Ala Lys Leu Arg Lys Val Ser Lys Gln
                485                 490                 495

GAG GAG GCC TCA GGG GGG CCC ACA GCC CCC AAA GCT GAG AGT GGT CGA    1536
Glu Glu Ala Ser Gly Gly Pro Thr Ala Pro Lys Ala Glu Ser Gly Arg
            500                 505                 510

AGC GGA GGT GGG GGA CTC ATG GAA GAG ATG AAC GCC ATG CTG GCC CGG    1584
Ser Gly Gly Gly Gly Leu Met Glu Glu Met Asn Ala Met Leu Ala Arg
        515                 520                 525

AGA AGG AAA GCC ACG CAA GTT GGG GAG AAA ACC CCC AAG GAT GAA TCT    1632
Arg Arg Lys Ala Thr Gln Val Gly Glu Lys Thr Pro Lys Asp Glu Ser
    530                 535                 540

GCC AAT CAG GAG GAG CCA GAG GCC AGA GTC CCG GCC CAG AGT GAA TCT    1680
Ala Asn Gln Glu Glu Pro Glu Ala Arg Val Pro Ala Gln Ser Glu Ser
545                 550                 555                 560

GTG CGG AGA CCC TGG GAG AAG AAC AGC ACA ACC TTG CCA AGG ATG AAG    1728
Val Arg Arg Pro Trp Glu Lys Asn Ser Thr Thr Leu Pro Arg Met Lys
                565                 570                 575

TCG TCT TCT TCG GTG ACC ACT TCC GAG ACC CAA CCC TGC ACG CCC AGC    1776
Ser Ser Ser Ser Val Thr Thr Ser Glu Thr Gln Pro Cys Thr Pro Ser
            580                 585                 590

TCC AGT GAT TAC TCG GAC CTA CAG AGG GTG AAA CAG GAG CTT CTG GAA    1824
Ser Ser Asp Tyr Ser Asp Leu Gln Arg Val Lys Gln Glu Leu Leu Glu
        595                 600                 605

GAG GTG AAG AAG GAA TTG CAG AAA GTG AAA GAG GAA ATC ATT GAA GCC    1872
Glu Val Lys Lys Glu Leu Gln Lys Val Lys Glu Glu Ile Ile Glu Ala
    610                 615                 620

TTC GTC CAG GAG CTG AGG AAG CGG GGT TCT CCC TGA                    1908
```

Phe Val Gln Glu Leu Arg Lys Arg Gly Ser Pro
625 630 635

(2) INFORMATION FOR SEQ ID NO:125:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 635 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:125:

Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
1 5 10 15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
20 25 30
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
35 40 45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
50 55 60
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65 70 75 80
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
85 90 95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
100 105 110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
115 120 125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
130 135 140
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145 150 155 160
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
165 170 175
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
180 185 190
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
195 200 205
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
210 215 220
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225 230 235 240
Gly Leu Arg Ser Arg Ala Gln Ala Ser Met Ser Glu Thr Val Ile Met
245 250 255
Ser Glu Thr Val Ile Cys Ser Ser Arg Ala Thr Val Met Leu Tyr Asp
260 265 270
Asp Gly Asn Lys Arg Trp Leu Pro Ala Gly Thr Gly Pro Gln Ala Phe
275 280 285
Ser Arg Val Gln Ile Tyr His Asn Pro Thr Ala Asn Ser Phe Arg Val
290 295 300
Val Gly Arg Lys Met Gln Pro Asp Gln Gln Val Val Ile Asn Cys Ala

305 310 315 320
Ile Val Arg Gly Val Lys Tyr Asn Gln Ala Thr Pro Asn Phe His Gln
325 330 335
Trp Arg Asp Ala Arg Gln Val Trp Gly Leu Asn Phe Gly Ser Lys Glu
340 345 350
Asp Ala Ala Gln Phe Ala Ala Gly Met Ala Ser Ala Leu Glu Ala Leu
355 360 365
Glu Gly Gly Gly Pro Pro Pro Pro Pro Ala Leu Pro Thr Trp Ser Val
370 375 380
Pro Asn Gly Pro Ser Pro Glu Glu Val Glu Gln Gln Lys Arg Gln Gln
385 390 395 400
Pro Gly Pro Ser Glu His Ile Glu Arg Arg Val Ser Asn Ala Gly Gly
405 410 415
Pro Pro Ala Pro Pro Ala Gly Gly Pro Pro Pro Pro Pro Gly Pro Pro
420 425 430
Pro Pro Pro Gly Pro Pro Pro Pro Pro Gly Leu Pro Pro Ser Gly Val
435 440 445
Pro Ala Ala Ala His Gly Ala Gly Gly Gly Pro Pro Pro Ala Pro Pro
450 455 460
Leu Pro Ala Ala Gln Gly Pro Gly Gly Gly Gly Ala Gly Ala Pro Gly
465 470 475 480
Leu Ala Ala Ala Ile Ala Gly Ala Lys Leu Arg Lys Val Ser Lys Gln
485 490 495
Glu Glu Ala Ser Gly Gly Pro Thr Ala Pro Lys Ala Glu Ser Gly Arg
500 505 510
Ser Gly Gly Gly Gly Leu Met Glu Glu Met Asn Ala Met Leu Ala Arg
515 520 525
Arg Arg Lys Ala Thr Gln Val Gly Glu Lys Thr Pro Lys Asp Glu Ser
530 535 540
Ala Asn Gln Glu Glu Pro Glu Ala Arg Val Pro Ala Gln Ser Glu Ser
545 550 555 560
Val Arg Arg Pro Trp Glu Lys Asn Ser Thr Thr Leu Pro Arg Met Lys
565 570 575
Ser Ser Ser Ser Val Thr Thr Ser Glu Thr Gln Pro Cys Thr Pro Ser
580 585 590
Ser Ser Asp Tyr Ser Asp Leu Gln Arg Val Lys Gln Glu Leu Leu Glu
595 600 605
Glu Val Lys Lys Glu Leu Gln Lys Val Lys Glu Glu Ile Ile Glu Ala
610 615 620
Phe Val Gln Glu Leu Arg Lys Arg Gly Ser Pro
625 630 635

(2) INFORMATION FOR SEQ ID NO:126:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1329 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...1326
(D) OTHER INFORMATION:

BNSDOCID: <WO___9845704A2_I_>

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:126:

```
ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15

GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30

GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45

TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC     192
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60

CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG     240
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80

CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG     288
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95

CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG     336
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110

GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC     384
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125

ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC     432
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140

AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC     480
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160

GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC     528
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175

GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC     576
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190

CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG     624
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205

AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC     672
```


BNSDOCID: <WO___9845704A2_I_>

```
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220

GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC     720
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240

GGA CTC AGA TCT CGA GCT CAA GCT TCA ATG GCT GCC ATC CGG AAG AAA     768
Gly Leu Arg Ser Arg Ala Gln Ala Ser Met Ala Ala Ile Arg Lys Lys
                245                 250                 255

CTG GTG ATT GTT GGT GAT GGA GCC TGT GGA AAG ACA TGC TTG CTC ATA     816
Leu Val Ile Val Gly Asp Gly Ala Cys Gly Lys Thr Cys Leu Leu Ile
            260                 265                 270

GTC TTC AGC AAG GAC CAG TTC CCA GAG GTG TAT GTG CCC ACA GTG TTT     864
Val Phe Ser Lys Asp Gln Phe Pro Glu Val Tyr Val Pro Thr Val Phe
        275                 280                 285

GAG AAC TAT GTG GCA GAT ATC GAG GTG GAT GGA AAG CAG GTA GAG TTG     912
Glu Asn Tyr Val Ala Asp Ile Glu Val Asp Gly Lys Gln Val Glu Leu
    290                 295                 300

GCT TTG TGG GAC ACA GCT GGG CAG GAA GAT TAT GAT CGC CTG AGG CCC     960
Ala Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr Asp Arg Leu Arg Pro
305                 310                 315                 320

CTC TCC TAC CCA GAT ACC GAT GTT ATA CTG ATG TGT TTT TCC ATC GAC    1008
Leu Ser Tyr Pro Asp Thr Asp Val Ile Leu Met Cys Phe Ser Ile Asp
                325                 330                 335

AGC CCT GAT AGT TTA GAA AAC ATC CCA GAA AAG TGG ACC CCA GAA GTC    1056
Ser Pro Asp Ser Leu Glu Asn Ile Pro Glu Lys Trp Thr Pro Glu Val
            340                 345                 350

AAG CAT TTC TGT CCC AAC GTG CCC ATC ATC CTG GTT GGG AAT AAG AAG    1104
Lys His Phe Cys Pro Asn Val Pro Ile Ile Leu Val Gly Asn Lys Lys
        355                 360                 365

GAT CTT CGG AAT GAT GAG CAC ACA AGG CGG GAG CTA GCC AAG ATG AAG    1152
Asp Leu Arg Asn Asp Glu His Thr Arg Arg Glu Leu Ala Lys Met Lys
    370                 375                 380

CAG GAG CCG GTG AAA CCT GAA GAA GGC AGA GAT ATG GCA AAC AGG ATT    1200
Gln Glu Pro Val Lys Pro Glu Glu Gly Arg Asp Met Ala Asn Arg Ile
385                 390                 395                 400

GGC GCT TTT GGG TAC ATG GAG TGT TCA GCA AAG ACC AAA GAT GGA GTG    1248
Gly Ala Phe Gly Tyr Met Glu Cys Ser Ala Lys Thr Lys Asp Gly Val
                405                 410                 415

AGA GAG GTT TTT GAA ATG GCT ACG AGA GCT GCT CTG CAA GCT AGA CGT    1296
Arg Glu Val Phe Glu Met Ala Thr Arg Ala Ala Leu Gln Ala Arg Arg
            420                 425                 430

GGG AAG AAA AAA TCT GGT TGC CTT GTC TTG TGA                        1329
```

Gly Lys Lys Lys Ser Gly Cys Leu Val Leu
435 440

(2) INFORMATION FOR SEQ ID NO:127:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 442 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:127:

Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
1 5 10 15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
20 25 30
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
35 40 45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
50 55 60
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65 70 75 80
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
85 90 95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
100 105 110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
115 120 125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
130 135 140
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145 150 155 160
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
165 170 175
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
180 185 190
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
195 200 205
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
210 215 220
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225 230 235 240
Gly Leu Arg Ser Arg Ala Gln Ala Ser Met Ala Ala Ile Arg Lys Lys
245 250 255
Leu Val Ile Val Gly Asp Gly Ala Cys Gly Lys Thr Cys Leu Leu Ile
260 265 270
Val Phe Ser Lys Asp Gln Phe Pro Glu Val Tyr Val Pro Thr Val Phe
275 280 285
Glu Asn Tyr Val Ala Asp Ile Glu Val Asp Gly Lys Gln Val Glu Leu
290 295 300
Ala Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr Asp Arg Leu Arg Pro

```
305                 310                 315                 320
Leu Ser Tyr Pro Asp Thr Asp Val Ile Leu Met Cys Phe Ser Ile Asp
                325                 330                 335
Ser Pro Asp Ser Leu Glu Asn Ile Pro Glu Lys Trp Thr Pro Glu Val
            340                 345                 350
Lys His Phe Cys Pro Asn Val Pro Ile Ile Leu Val Gly Asn Lys Lys
        355                 360                 365
Asp Leu Arg Asn Asp Glu His Thr Arg Arg Glu Leu Ala Lys Met Lys
    370                 375                 380
Gln Glu Pro Val Lys Pro Glu Glu Gly Arg Asp Met Ala Asn Arg Ile
385                 390                 395                 400
Gly Ala Phe Gly Tyr Met Glu Cys Ser Ala Lys Thr Lys Asp Gly Val
                405                 410                 415
Arg Glu Val Phe Glu Met Ala Thr Arg Ala Ala Leu Gln Ala Arg Arg
            420                 425                 430
Gly Lys Lys Lys Ser Gly Cys Leu Val Leu
        435                 440
```

(2) INFORMATION FOR SEQ ID NO:128:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1140 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...1137
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:128:

```
ATG GAC CAT TAT GAT TCT CAG CAA ACC AAC GAT TAC ATG CAG CCA GAA      48
Met Asp His Tyr Asp Ser Gln Gln Thr Asn Asp Tyr Met Gln Pro Glu
 1               5                  10                  15

GAG GAC TGG GAC CGG GAC CTG CTC CTG GAC CCG GCC TGG GAG AAG CAG      96
Glu Asp Trp Asp Arg Asp Leu Leu Leu Asp Pro Ala Trp Glu Lys Gln
            20                  25                  30

CAG AGA AAG ACA TTC ACG GCA TGG TGT AAC TCC CAC CTC CGG AAG GCG     144
Gln Arg Lys Thr Phe Thr Ala Trp Cys Asn Ser His Leu Arg Lys Ala
        35                  40                  45

GGG ACA CAG ATC GAG AAC ATC GAA GAG GAC TTC CGG GAT GGC CTG AAG     192
Gly Thr Gln Ile Glu Asn Ile Glu Glu Asp Phe Arg Asp Gly Leu Lys
    50                  55                  60

CTC ATG CTG CTG CTG GAG GTC ATC TCA GGT GAA CGC TTG GCC AAG CCA     240
Leu Met Leu Leu Leu Glu Val Ile Ser Gly Glu Arg Leu Ala Lys Pro
65                  70                  75                  80

GAG CGA GGC AAG ATG AGA GTG CAC AAG ATC TCC AAC GTC AAC AAG GCC     288
```

250

```
Glu Arg Gly Lys Met Arg Val His Lys Ile Ser Asn Val Asn Lys Ala
                85                  90                  95

CTG GAT TTC ATA GCC AGC AAA GGC GTC AAA CTG GTG TCC ATC GGA GCC      336
Leu Asp Phe Ile Ala Ser Lys Gly Val Lys Leu Val Ser Ile Gly Ala
            100                 105                 110

GAA GAA ATC GTG GAT GGG AAT GTG AAG ATG ACC CTG GGC ATG ATC TGG      384
Glu Glu Ile Val Asp Gly Asn Val Lys Met Thr Leu Gly Met Ile Trp
        115                 120                 125

ACC ATC ATC CTG CGC AGG GAT CCA CCG GTC GCC ACC ATG GTG AGC AAG      432
Thr Ile Ile Leu Arg Arg Asp Pro Pro Val Ala Thr Met Val Ser Lys
    130                 135                 140

GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG GTC GAG CTG GAC      480
Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp
145                 150                 155                 160

GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC GAG GGC GAG GGC      528
Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly
                165                 170                 175

GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC TGC ACC ACC GGC      576
Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly
            180                 185                 190

AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC CTG ACC TAC GGC      624
Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Thr Tyr Gly
        195                 200                 205

GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG CAG CAC GAC TTC      672
Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln His Asp Phe
    210                 215                 220

TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG CGC ACC ATC TTC      720
Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe
225                 230                 235                 240

TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG GTG AAG TTC GAG      768
Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu
                245                 250                 255

GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC ATC GAC TTC AAG      816
Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys
            260                 265                 270

GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC AAC TAC AAC AGC      864
Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser
        275                 280                 285

CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC GGC ATC AAG GTG      912
His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val
    290                 295                 300

AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC GTG CAG CTC GCC      960
```

250

```
Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala
305                 310                 315                 320

GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC CCC GTG CTG CTG    1008
Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu
                325                 330                 335

CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG AGC AAA GAC CCC    1056
Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro
            340                 345                 350

AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC GTG ACC GCC GCC    1104
Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala
        355                 360                 365

GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TAA                    1140
Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
    370                 375
```

(2) INFORMATION FOR SEQ ID NO:129:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 379 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:129:

```
Met Asp His Tyr Asp Ser Gln Gln Thr Asn Asp Tyr Met Gln Pro Glu
 1               5                  10                  15
Glu Asp Trp Asp Arg Asp Leu Leu Leu Asp Pro Ala Trp Glu Lys Gln
            20                  25                  30
Gln Arg Lys Thr Phe Thr Ala Trp Cys Asn Ser His Leu Arg Lys Ala
        35                  40                  45
Gly Thr Gln Ile Glu Asn Ile Glu Glu Asp Phe Arg Asp Gly Leu Lys
    50                  55                  60
Leu Met Leu Leu Leu Glu Val Ile Ser Gly Glu Arg Leu Ala Lys Pro
65                  70                  75                  80
Glu Arg Gly Lys Met Arg Val His Lys Ile Ser Asn Val Asn Lys Ala
                85                  90                  95
Leu Asp Phe Ile Ala Ser Lys Gly Val Lys Leu Val Ser Ile Gly Ala
            100                 105                 110
Glu Glu Ile Val Asp Gly Asn Val Lys Met Thr Leu Gly Met Ile Trp
        115                 120                 125
Thr Ile Ile Leu Arg Arg Asp Pro Pro Val Ala Thr Met Val Ser Lys
    130                 135                 140
Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp
145                 150                 155                 160
Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly
                165                 170                 175
Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly
```

```
                180                 185                 190
Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Thr Tyr Gly
        195                 200                 205
Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln His Asp Phe
    210                 215                 220
Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe
225                 230                 235                 240
Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu
                245                 250                 255
Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys
            260                 265                 270
Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser
        275                 280                 285
His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val
    290                 295                 300
Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala
305                 310                 315                 320
Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu
                325                 330                 335
Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro
            340                 345                 350
Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala
        355                 360                 365
Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
    370                 375
```

(2) INFORMATION FOR SEQ ID NO:130:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3516 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...3513
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:130:

```
ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15

GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30

GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45

TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC     192
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Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60

CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG     240
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80

CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG     288
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95

CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG     336
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110

GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC     384
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125

ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC     432
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140

AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC     480
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160

GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC     528
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175

GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC     576
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190

CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG     624
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205

AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC     672
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220

GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC     720
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240

GGA CTC AGA TCT CGA GCC ATG AAC GCC CCC GAG CGG CAG CCC CAA CCC     768
Gly Leu Arg Ser Arg Ala Met Asn Ala Pro Glu Arg Gln Pro Gln Pro
                245                 250                 255

GAC GGC GGG GAC GCC CCA GGC CAC GAG CCT GGG GGC AGC CCC CAA GAC     816
Asp Gly Gly Asp Ala Pro Gly His Glu Pro Gly Gly Ser Pro Gln Asp
            260                 265                 270

GAG CTT GAC TTC TCC ATC CTC TTC GAC TAT GAG TAT TTG AAT CCG AAC     864
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```
Glu Leu Asp Phe Ser Ile Leu Phe Asp Tyr Glu Tyr Leu Asn Pro Asn
        275                 280                 285

GAA GAA GAG CCG AAT GCA CAT AAG GTC GCC AGC CCA CCC TCC GGA CCC      912
Glu Glu Glu Pro Asn Ala His Lys Val Ala Ser Pro Pro Ser Gly Pro
    290                 295                 300

GCA TAC CCC GAT GAT GTA ATG GAC TAT GGC CTC AAG CCA TAC AGC CCC      960
Ala Tyr Pro Asp Asp Val Met Asp Tyr Gly Leu Lys Pro Tyr Ser Pro
305                 310                 315                 320

CTT GCT AGT CTC TCT GGC GAG CCC CCC GGC CGA TTC GGA GAG CCG GAT     1008
Leu Ala Ser Leu Ser Gly Glu Pro Pro Gly Arg Phe Gly Glu Pro Asp
                325                 330                 335

AGG GTA GGG CCG CAG AAG TTT CTG AGC GCG GCC AAG CCA GCA GGG GCC     1056
Arg Val Gly Pro Gln Lys Phe Leu Ser Ala Ala Lys Pro Ala Gly Ala
            340                 345                 350

TCG GGC CTG AGC CCT CGG ATC GAG ATC ACT CCG TCC CAC GAA CTG ATC     1104
Ser Gly Leu Ser Pro Arg Ile Glu Ile Thr Pro Ser His Glu Leu Ile
        355                 360                 365

CAG GCA GTG GGG CCC CTC CGC ATG AGA GAC GCG GGC CTC CTG GTG GAG     1152
Gln Ala Val Gly Pro Leu Arg Met Arg Asp Ala Gly Leu Leu Val Glu
    370                 375                 380

CAG CCT CCC CTG GCC GGG GTG GCC GCC AGC CCG AGG TTC ACC CTG CCC     1200
Gln Pro Pro Leu Ala Gly Val Ala Ala Ser Pro Arg Phe Thr Leu Pro
385                 390                 395                 400

GTG CCC GGC TTC GAG GGC TAC CGC GAG CCG CTT TGC TTG AGC CCC GCT     1248
Val Pro Gly Phe Glu Gly Tyr Arg Glu Pro Leu Cys Leu Ser Pro Ala
                405                 410                 415

AGC AGC GGC TCC TCT GCC AGC TTC ATT TCT GAC ACC TTC TCC CCC TAC     1296
Ser Ser Gly Ser Ser Ala Ser Phe Ile Ser Asp Thr Phe Ser Pro Tyr
            420                 425                 430

ACC TCG CCC TGC GTC TCG CCC AAT AAC GGC GGG CCC GAC GAC CTG TGT     1344
Thr Ser Pro Cys Val Ser Pro Asn Asn Gly Gly Pro Asp Asp Leu Cys
        435                 440                 445

CCG CAG TTT CAA AAC ATC CCT GCT CAT TAT TCC CCC AGA ACC TCG CCA     1392
Pro Gln Phe Gln Asn Ile Pro Ala His Tyr Ser Pro Arg Thr Ser Pro
    450                 455                 460

ATA ATG TCA CCT CGA ACC AGC CTC GCC GAG GAC AGC TGC CTG GGC CGC     1440
Ile Met Ser Pro Arg Thr Ser Leu Ala Glu Asp Ser Cys Leu Gly Arg
465                 470                 475                 480

CAC TCG CCC GTG CCC CGT CCG GCC TCC CGC TCC TCA TCG CCT GGT GCC     1488
His Ser Pro Val Pro Arg Pro Ala Ser Arg Ser Ser Ser Pro Gly Ala
                485                 490                 495

AAG CGG AGG CAT TCG TGC GCC GAG GCC TTG GTT GCC CTG CCG CCC GGA     1536
```

```
Lys Arg Arg His Ser Cys Ala Glu Ala Leu Val Ala Leu Pro Pro Gly
            500                 505                 510

GCC TCA CCC CAG CGC TCC CGG AGC CCC TCG CCG CAG CCC TCA TCT CAC    1584
Ala Ser Pro Gln Arg Ser Arg Ser Pro Ser Pro Gln Pro Ser Ser His
        515                 520                 525

GTG GCA CCC CAG GAC CAC GGC TCC CCG GCT GGG TAC CCC CCT GTG GCT    1632
Val Ala Pro Gln Asp His Gly Ser Pro Ala Gly Tyr Pro Pro Val Ala
    530                 535                 540

GGC TCT GCC GTG ATC ATG GAT GCC CTG AAC AGC CTC GCC ACG GAC TCG    1680
Gly Ser Ala Val Ile Met Asp Ala Leu Asn Ser Leu Ala Thr Asp Ser
545                 550                 555                 560

CCT TGT GGG ATC CCC CCC AAG ATG TGG AAG ACC AGC CCT GAC CCC TCG    1728
Pro Cys Gly Ile Pro Pro Lys Met Trp Lys Thr Ser Pro Asp Pro Ser
                565                 570                 575

CCG GTG TCT GCC GCC CCA TCC AAG GCC GGC CTG CCT CGC CAC ATC TAC    1776
Pro Val Ser Ala Ala Pro Ser Lys Ala Gly Leu Pro Arg His Ile Tyr
            580                 585                 590

CCG GCC GTG GAG TTC CTG GGG CCC TGC GAG CAG GGC GAG AGG AGA AAC    1824
Pro Ala Val Glu Phe Leu Gly Pro Cys Glu Gln Gly Glu Arg Arg Asn
        595                 600                 605

TCG GCT CCA GAA TCC ATC CTG CTG GTT CCG CCC ACT TGG CCC AAG CCG    1872
Ser Ala Pro Glu Ser Ile Leu Leu Val Pro Pro Thr Trp Pro Lys Pro
    610                 615                 620

CTG GTG CCT GCC ATT CCC ATC TGC AGC ATC CCA GTG ACT GCA TCC CTC    1920
Leu Val Pro Ala Ile Pro Ile Cys Ser Ile Pro Val Thr Ala Ser Leu
625                 630                 635                 640

CCT CCA CTT GAG TGG CCG CTG TCC AGT CAG TCA GGC TCT TAC GAG CTG    1968
Pro Pro Leu Glu Trp Pro Leu Ser Ser Gln Ser Gly Ser Tyr Glu Leu
                645                 650                 655

CGG ATC GAG GTG CAG CCC AAG CCA CAT CAC CGG GCC CAC TAT GAG ACA    2016
Arg Ile Glu Val Gln Pro Lys Pro His His Arg Ala His Tyr Glu Thr
            660                 665                 670

GAA GGC AGC CGA GGG GCT GTC AAA GCT CCA ACT GGA GGC CAC CCT GTG    2064
Glu Gly Ser Arg Gly Ala Val Lys Ala Pro Thr Gly Gly His Pro Val
        675                 680                 685

GTT CAG CTC CAT GGC TAC ATG GAA AAC AAG CCT CTG GGA CTT CAG ATC    2112
Val Gln Leu His Gly Tyr Met Glu Asn Lys Pro Leu Gly Leu Gln Ile
    690                 695                 700

TTC ATT GGG ACA GCT GAT GAG CGG ATC CTT AAG CCG CAC GCC TTC TAC    2160
Phe Ile Gly Thr Ala Asp Glu Arg Ile Leu Lys Pro His Ala Phe Tyr
705                 710                 715                 720

CAG GTG CAC CGA ATC ACG GGG AAA ACT GTC ACC ACC ACC AGC TAT GAG    2208
```

```
Gln Val His Arg Ile Thr Gly Lys Thr Val Thr Thr Thr Ser Tyr Glu
                725                 730                 735

AAG ATA GTG GGC AAC ACC AAA GTC CTG GAG ATC CCC TTG GAG CCC AAA    2256
Lys Ile Val Gly Asn Thr Lys Val Leu Glu Ile Pro Leu Glu Pro Lys
            740                 745                 750

AAC AAC ATG AGG GCA ACC ATC GAC TGT GCG GGG ATC TTG AAG CTT AGA    2304
Asn Asn Met Arg Ala Thr Ile Asp Cys Ala Gly Ile Leu Lys Leu Arg
        755                 760                 765

AAC GCC GAC ATT GAG CTG CGG AAA GGC GAG ACG GAC ATT GGA AGA AAG    2352
Asn Ala Asp Ile Glu Leu Arg Lys Gly Glu Thr Asp Ile Gly Arg Lys
    770                 775                 780

AAC ACG CGG GTG AGA CTG GTT TTC CGA GTT CAC ATC CCA GAG TCC AGT    2400
Asn Thr Arg Val Arg Leu Val Phe Arg Val His Ile Pro Glu Ser Ser
785                 790                 795                 800

GGC AGA ATC GTC TCT TTA CAG ACT GCA TCT AAC CCC ATC GAG TGC TCC    2448
Gly Arg Ile Val Ser Leu Gln Thr Ala Ser Asn Pro Ile Glu Cys Ser
                805                 810                 815

CAG CGA TCT GCT CAC GAG CTG CCC ATG GTT GAA AGA CAA GAC ACA GAC    2496
Gln Arg Ser Ala His Glu Leu Pro Met Val Glu Arg Gln Asp Thr Asp
            820                 825                 830

AGC TGC CTG GTC TAT GGC GGC CAG CAA ATG ATC CTC ACG GGG CAG AAC    2544
Ser Cys Leu Val Tyr Gly Gly Gln Gln Met Ile Leu Thr Gly Gln Asn
        835                 840                 845

TTT ACA TCC GAG TCC AAA GTT GTG TTT ACT GAG AAG ACC ACA GAT GGA    2592
Phe Thr Ser Glu Ser Lys Val Val Phe Thr Glu Lys Thr Thr Asp Gly
    850                 855                 860

CAG CAA ATT TGG GAG ATG GAA GCC ACG GTG GAT AAG GAC AAG AGC CAG    2640
Gln Gln Ile Trp Glu Met Glu Ala Thr Val Asp Lys Asp Lys Ser Gln
865                 870                 875                 880

CCC AAC ATG CTT TTT GTT GAG ATC CCT GAA TAT CGG AAC AAG CAT ATC    2688
Pro Asn Met Leu Phe Val Glu Ile Pro Glu Tyr Arg Asn Lys His Ile
                885                 890                 895

CGC ACA CCT GTA AAA GTG AAC TTC TAC GTC ATC AAT GGG AAG AGA AAA    2736
Arg Thr Pro Val Lys Val Asn Phe Tyr Val Ile Asn Gly Lys Arg Lys
            900                 905                 910

CGA AGT CAG CCT CAG CAC TTT ACC TAC CAC CCA GTC CCA GCC ATC AAG    2784
Arg Ser Gln Pro Gln His Phe Thr Tyr His Pro Val Pro Ala Ile Lys
        915                 920                 925

ACG GAG CCC ACG GAT GAA TAT GAC CCC ACT CTG ATC TGC AGC CCC ACC    2832
Thr Glu Pro Thr Asp Glu Tyr Asp Pro Thr Leu Ile Cys Ser Pro Thr
    930                 935                 940

CAT GGA GGC CTG GGG AGC CAG CCT TAC TAC CCC CAG CAC CCG ATG GTG    2880
```

```
His Gly Gly Leu Gly Ser Gln Pro Tyr Tyr Pro Gln His Pro Met Val
945                 950                 955                 960

GCC GAG TCC CCC TCC TGC CTC GTG GCC ACC ATG GCT CCC TGC CAG CAG    2928
Ala Glu Ser Pro Ser Cys Leu Val Ala Thr Met Ala Pro Cys Gln Gln
                965                 970                 975

TTC CGC ACG GGG CTC TCA TCC CCT GAC GCC CGC TAC CAG CAA CAG AAC    2976
Phe Arg Thr Gly Leu Ser Ser Pro Asp Ala Arg Tyr Gln Gln Gln Asn
            980                 985                 990

CCA GCG GCC GTA CTC TAC CAG CGG AGC AAG AGC CTG AGC CCC AGC CTG    3024
Pro Ala Ala Val Leu Tyr Gln Arg Ser Lys Ser Leu Ser Pro Ser Leu
        995                1000                1005

CTG GGC TAT CAG CAG CCG GCC CTC ATG GCC GCC CCG CTG TCC CTT GCG    3072
Leu Gly Tyr Gln Gln Pro Ala Leu Met Ala Ala Pro Leu Ser Leu Ala
    1010                1015                1020

GAC GCT CAC CGC TCT GTG CTG GTG CAC GCC GGC TCC CAG GGC CAG AGC    3120
Asp Ala His Arg Ser Val Leu Val His Ala Gly Ser Gln Gly Gln Ser
1025                1030                1035                1040

TCA GCC CTG CTC CAC CCC TCT CCG ACC AAC CAG CAG GCC TCG CCT GTG    3168
Ser Ala Leu Leu His Pro Ser Pro Thr Asn Gln Gln Ala Ser Pro Val
                1045                1050                1055

ATC CAC TAC TCA CCC ACC AAC CAG CAG CTG CGC TGC GGA AGC CAC CAG    3216
Ile His Tyr Ser Pro Thr Asn Gln Gln Leu Arg Cys Gly Ser His Gln
            1060                1065                1070

GAG TTC CAG CAC ATC ATG TAC TGC GAG AAT TTC GCA CCA GGC ACC ACC    3264
Glu Phe Gln His Ile Met Tyr Cys Glu Asn Phe Ala Pro Gly Thr Thr
        1075                1080                1085

AGA CCT GGC CCG CCC CCG GTC AGT CAA GGT CAG AGG CTG AGC CCG GGT    3312
Arg Pro Gly Pro Pro Pro Val Ser Gln Gly Gln Arg Leu Ser Pro Gly
    1090                1095                1100

TCC TAC CCC ACA GTC ATT CAG CAG CAG AAT GCC ACG AGC CAA AGA GCC    3360
Ser Tyr Pro Thr Val Ile Gln Gln Gln Asn Ala Thr Ser Gln Arg Ala
1105                1110                1115                1120

GCC AAA AAC GGA CCC CCG GTC AGT GAC CAA AAG GAA GTA TTA CCT GCG    3408
Ala Lys Asn Gly Pro Pro Val Ser Asp Gln Lys Glu Val Leu Pro Ala
                1125                1130                1135

GGG GTG ACC ATT AAA CAG GAG CAG AAC TTG GAC CAG ACC TAC TTG GAT    3456
Gly Val Thr Ile Lys Gln Glu Gln Asn Leu Asp Gln Thr Tyr Leu Asp
            1140                1145                1150

GAT GTT AAT GAA ATT ATC AGG AAG GAG TTT TCA GGA CCT CCT GCC AGA    3504
Asp Val Asn Glu Ile Ile Arg Lys Glu Phe Ser Gly Pro Pro Ala Arg
        1155                1160                1165

AAT CAG ACG TAA                                                   3516
```

Asn Gln Thr
1170

(2) INFORMATION FOR SEQ ID NO:131:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1171 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:131:

```
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240
Gly Leu Arg Ser Arg Ala Met Asn Ala Pro Glu Arg Gln Pro Gln Pro
                245                 250                 255
Asp Gly Gly Asp Ala Pro Gly His Glu Pro Gly Gly Ser Pro Gln Asp
            260                 265                 270
Glu Leu Asp Phe Ser Ile Leu Phe Asp Tyr Glu Tyr Leu Asn Pro Asn
        275                 280                 285
Glu Glu Glu Pro Asn Ala His Lys Val Ala Ser Pro Pro Ser Gly Pro
    290                 295                 300
Ala Tyr Pro Asp Asp Val Met Asp Tyr Gly Leu Lys Pro Tyr Ser Pro
```

305 310 315 320
Leu Ala Ser Leu Ser Gly Glu Pro Pro Gly Arg Phe Gly Glu Pro Asp
325 330 335
Arg Val Gly Pro Gln Lys Phe Leu Ser Ala Ala Lys Pro Ala Gly Ala
340 345 350
Ser Gly Leu Ser Pro Arg Ile Glu Ile Thr Pro Ser His Glu Leu Ile
355 360 365
Gln Ala Val Gly Pro Leu Arg Met Arg Asp Ala Gly Leu Leu Val Glu
370 375 380
Gln Pro Pro Leu Ala Gly Val Ala Ala Ser Pro Arg Phe Thr Leu Pro
385 390 395 400
Val Pro Gly Phe Glu Gly Tyr Arg Glu Pro Leu Cys Leu Ser Pro Ala
405 410 415
Ser Ser Gly Ser Ser Ala Ser Phe Ile Ser Asp Thr Phe Ser Pro Tyr
420 425 430
Thr Ser Pro Cys Val Ser Pro Asn Asn Gly Gly Pro Asp Asp Leu Cys
435 440 445
Pro Gln Phe Gln Asn Ile Pro Ala His Tyr Ser Pro Arg Thr Ser Pro
450 455 460
Ile Met Ser Pro Arg Thr Ser Leu Ala Glu Asp Ser Cys Leu Gly Arg
465 470 475 480
His Ser Pro Val Pro Arg Pro Ala Ser Arg Ser Ser Ser Pro Gly Ala
485 490 495
Lys Arg Arg His Ser Cys Ala Glu Ala Leu Val Ala Leu Pro Pro Gly
500 505 510
Ala Ser Pro Gln Arg Ser Arg Ser Pro Ser Pro Gln Pro Ser Ser His
515 520 525
Val Ala Pro Gln Asp His Gly Ser Pro Ala Gly Tyr Pro Pro Val Ala
530 535 540
Gly Ser Ala Val Ile Met Asp Ala Leu Asn Ser Leu Ala Thr Asp Ser
545 550 555 560
Pro Cys Gly Ile Pro Pro Lys Met Trp Lys Thr Ser Pro Asp Pro Ser
565 570 575
Pro Val Ser Ala Ala Pro Ser Lys Ala Gly Leu Pro Arg His Ile Tyr
580 585 590
Pro Ala Val Glu Phe Leu Gly Pro Cys Glu Gln Gly Glu Arg Arg Asn
595 600 605
Ser Ala Pro Glu Ser Ile Leu Leu Val Pro Pro Thr Trp Pro Lys Pro
610 615 620
Leu Val Pro Ala Ile Pro Ile Cys Ser Ile Pro Val Thr Ala Ser Leu
625 630 635 640
Pro Pro Leu Glu Trp Pro Leu Ser Ser Gln Ser Gly Ser Tyr Glu Leu
645 650 655
Arg Ile Glu Val Gln Pro Lys Pro His His Arg Ala His Tyr Glu Thr
660 665 670
Glu Gly Ser Arg Gly Ala Val Lys Ala Pro Thr Gly Gly His Pro Val
675 680 685
Val Gln Leu His Gly Tyr Met Glu Asn Lys Pro Leu Gly Leu Gln Ile
690 695 700
Phe Ile Gly Thr Ala Asp Glu Arg Ile Leu Lys Pro His Ala Phe Tyr
705 710 715 720
Gln Val His Arg Ile Thr Gly Lys Thr Val Thr Thr Thr Ser Tyr Glu
725 730 735
Lys Ile Val Gly Asn Thr Lys Val Leu Glu Ile Pro Leu Glu Pro Lys
740 745 750
Asn Asn Met Arg Ala Thr Ile Asp Cys Ala Gly Ile Leu Lys Leu Arg

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          755                 760                 765
Asn Ala Asp Ile Glu Leu Arg Lys Gly Glu Thr Asp Ile Gly Arg Lys
      770                 775                 780
Asn Thr Arg Val Arg Leu Val Phe Arg Val His Ile Pro Glu Ser Ser
785                 790                 795                 800
Gly Arg Ile Val Ser Leu Gln Thr Ala Ser Asn Pro Ile Glu Cys Ser
                805                 810                 815
Gln Arg Ser Ala His Glu Leu Pro Met Val Glu Arg Gln Asp Thr Asp
            820                 825                 830
Ser Cys Leu Val Tyr Gly Gly Gln Gln Met Ile Leu Thr Gly Gln Asn
          835                 840                 845
Phe Thr Ser Glu Ser Lys Val Val Phe Thr Glu Lys Thr Thr Asp Gly
      850                 855                 860
Gln Gln Ile Trp Glu Met Glu Ala Thr Val Asp Lys Asp Lys Ser Gln
865                 870                 875                 880
Pro Asn Met Leu Phe Val Glu Ile Pro Glu Tyr Arg Asn Lys His Ile
                885                 890                 895
Arg Thr Pro Val Lys Val Asn Phe Tyr Val Ile Asn Gly Lys Arg Lys
            900                 905                 910
Arg Ser Gln Pro Gln His Phe Thr Tyr His Pro Val Pro Ala Ile Lys
          915                 920                 925
Thr Glu Pro Thr Asp Glu Tyr Asp Pro Thr Leu Ile Cys Ser Pro Thr
      930                 935                 940
His Gly Gly Leu Gly Ser Gln Pro Tyr Tyr Pro Gln His Pro Met Val
945                 950                 955                 960
Ala Glu Ser Pro Ser Cys Leu Val Ala Thr Met Ala Pro Cys Gln Gln
                965                 970                 975
Phe Arg Thr Gly Leu Ser Ser Pro Asp Ala Arg Tyr Gln Gln Gln Asn
            980                 985                 990
Pro Ala Ala Val Leu Tyr Gln Arg Ser Lys Ser Leu Ser Pro Ser Leu
          995                1000                1005
Leu Gly Tyr Gln Gln Pro Ala Leu Met Ala Ala Pro Leu Ser Leu Ala
     1010                1015                1020
Asp Ala His Arg Ser Val Leu Val His Ala Gly Ser Gln Gly Gln Ser
025                 1030                1035                1040
Ser Ala Leu Leu His Pro Ser Pro Thr Asn Gln Gln Ala Ser Pro Val
                1045                1050                1055
Ile His Tyr Ser Pro Thr Asn Gln Gln Leu Arg Cys Gly Ser His Gln
            1060                1065                1070
Glu Phe Gln His Ile Met Tyr Cys Glu Asn Phe Ala Pro Gly Thr Thr
        1075                1080                1085
Arg Pro Gly Pro Pro Pro Val Ser Gln Gly Gln Arg Leu Ser Pro Gly
    1090                1095                1100
Ser Tyr Pro Thr Val Ile Gln Gln Gln Asn Ala Thr Ser Gln Arg Ala
105                 1110                1115                1120
Ala Lys Asn Gly Pro Pro Val Ser Asp Gln Lys Glu Val Leu Pro Ala
                1125                1130                1135
Gly Val Thr Ile Lys Gln Glu Gln Asn Leu Asp Gln Thr Tyr Leu Asp
            1140                1145                1150
Asp Val Asn Glu Ile Ile Arg Lys Glu Phe Ser Gly Pro Pro Ala Arg
        1155                1160                1165
Asn Gln Thr
    1170
```

(2) INFORMATION FOR SEQ ID NO:132:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3546 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...3543
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:132:

```
ATG AAC GCC CCC GAG CGG CAG CCC CAA CCC GAC GGC GGG GAC GCC CCA      48
Met Asn Ala Pro Glu Arg Gln Pro Gln Pro Asp Gly Gly Asp Ala Pro
 1               5                  10                  15

GGC CAC GAG CCT GGG GGC AGC CCC CAA GAC GAG CTT GAC TTC TCC ATC      96
Gly His Glu Pro Gly Gly Ser Pro Gln Asp Glu Leu Asp Phe Ser Ile
            20                  25                  30

CTC TTC GAC TAT GAG TAT TTG AAT CCG AAC GAA GAA GAG CCG AAT GCA     144
Leu Phe Asp Tyr Glu Tyr Leu Asn Pro Asn Glu Glu Glu Pro Asn Ala
        35                  40                  45

CAT AAG GTC GCC AGC CCA CCC TCC GGA CCC GCA TAC CCC GAT GAT GTA     192
His Lys Val Ala Ser Pro Pro Ser Gly Pro Ala Tyr Pro Asp Asp Val
    50                  55                  60

ATG GAC TAT GGC CTC AAG CCA TAC AGC CCC CTT GCT AGT CTC TCT GGC     240
Met Asp Tyr Gly Leu Lys Pro Tyr Ser Pro Leu Ala Ser Leu Ser Gly
65                  70                  75                  80

GAG CCC CCC GGC CGA TTC GGA GAG CCG GAT AGG GTA GGG CCG CAG AAG     288
Glu Pro Pro Gly Arg Phe Gly Glu Pro Asp Arg Val Gly Pro Gln Lys
                85                  90                  95

TTT CTG AGC GCG GCC AAG CCA GCA GGG GCC TCG GGC CTG AGC CCT CGG     336
Phe Leu Ser Ala Ala Lys Pro Ala Gly Ala Ser Gly Leu Ser Pro Arg
            100                 105                 110

ATC GAG ATC ACT CCG TCC CAC GAA CTG ATC CAG GCA GTG GGG CCC CTC     384
Ile Glu Ile Thr Pro Ser His Glu Leu Ile Gln Ala Val Gly Pro Leu
        115                 120                 125

CGC ATG AGA GAC GCG GGC CTC CTG GTG GAG CAG CCT CCC CTG GCC GGG     432
Arg Met Arg Asp Ala Gly Leu Leu Val Glu Gln Pro Pro Leu Ala Gly
    130                 135                 140

GTG GCC GCC AGC CCG AGG TTC ACC CTG CCC GTG CCC GGC TTC GAG GGC     480
Val Ala Ala Ser Pro Arg Phe Thr Leu Pro Val Pro Gly Phe Glu Gly
145                 150                 155                 160

TAC CGC GAG CCG CTT TGC TTG AGC CCC GCT AGC AGC GGC TCC TCT GCC     528
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Tyr Arg Glu Pro Leu Cys Leu Ser Pro Ala Ser Ser Gly Ser Ser Ala
                165                 170                 175

AGC TTC ATT TCT GAC ACC TTC TCC CCC TAC ACC TCG CCC TGC GTC TCG     576
Ser Phe Ile Ser Asp Thr Phe Ser Pro Tyr Thr Ser Pro Cys Val Ser
            180                 185                 190

CCC AAT AAC GGC GGG CCC GAC GAC CTG TGT CCG CAG TTT CAA AAC ATC     624
Pro Asn Asn Gly Gly Pro Asp Asp Leu Cys Pro Gln Phe Gln Asn Ile
        195                 200                 205

CCT GCT CAT TAT TCC CCC AGA ACC TCG CCA ATA ATG TCA CCT CGA ACC     672
Pro Ala His Tyr Ser Pro Arg Thr Ser Pro Ile Met Ser Pro Arg Thr
    210                 215                 220

AGC CTC GCC GAG GAC AGC TGC CTG GGC CGC CAC TCG CCC GTG CCC CGT     720
Ser Leu Ala Glu Asp Ser Cys Leu Gly Arg His Ser Pro Val Pro Arg
225                 230                 235                 240

CCG GCC TCC CGC TCC TCA TCG CCT GGT GCC AAG CGG AGG CAT TCG TGC     768
Pro Ala Ser Arg Ser Ser Ser Pro Gly Ala Lys Arg Arg His Ser Cys
                245                 250                 255

GCC GAG GCC TTG GTT GCC CTG CCG CCC GGA GCC TCA CCC CAG CGC TCC     816
Ala Glu Ala Leu Val Ala Leu Pro Pro Gly Ala Ser Pro Gln Arg Ser
            260                 265                 270

CGG AGC CCC TCG CCG CAG CCC TCA TCT CAC GTG GCA CCC CAG GAC CAC     864
Arg Ser Pro Ser Pro Gln Pro Ser Ser His Val Ala Pro Gln Asp His
        275                 280                 285

GGC TCC CCG GCT GGG TAC CCC CCT GTG GCT GGC TCT GCC GTG ATC ATG     912
Gly Ser Pro Ala Gly Tyr Pro Pro Val Ala Gly Ser Ala Val Ile Met
    290                 295                 300

GAT GCC CTG AAC AGC CTC GCC ACG GAC TCG CCT TGT GGG ATC CCC CCC     960
Asp Ala Leu Asn Ser Leu Ala Thr Asp Ser Pro Cys Gly Ile Pro Pro
305                 310                 315                 320

AAG ATG TGG AAG ACC AGC CCT GAC CCC TCG CCG GTG TCT GCC GCC CCA    1008
Lys Met Trp Lys Thr Ser Pro Asp Pro Ser Pro Val Ser Ala Ala Pro
                325                 330                 335

TCC AAG GCC GGC CTG CCT CGC CAC ATC TAC CCG GCC GTG GAG TTC CTG    1056
Ser Lys Ala Gly Leu Pro Arg His Ile Tyr Pro Ala Val Glu Phe Leu
            340                 345                 350

GGG CCC TGC GAG CAG GGC GAG AGG AGA AAC TCG GCT CCA GAA TCC ATC    1104
Gly Pro Cys Glu Gln Gly Glu Arg Arg Asn Ser Ala Pro Glu Ser Ile
        355                 360                 365

CTG CTG GTT CCG CCC ACT TGG CCC AAG CCG CTG GTG CCT GCC ATT CCC    1152
Leu Leu Val Pro Pro Thr Trp Pro Lys Pro Leu Val Pro Ala Ile Pro
    370                 375                 380

ATC TGC AGC ATC CCA GTG ACT GCA TCC CTC CCT CCA CTT GAG TGG CCG    1200
```


BNSDOCID: <WO___9845704A2_I_>

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Ile Cys Ser Ile Pro Val Thr Ala Ser Leu Pro Pro Leu Glu Trp Pro
385                 390                 395                 400

CTG TCC AGT CAG TCA GGC TCT TAC GAG CTG CGG ATC GAG GTG CAG CCC    1248
Leu Ser Ser Gln Ser Gly Ser Tyr Glu Leu Arg Ile Glu Val Gln Pro
                405                 410                 415

AAG CCA CAT CAC CGG GCC CAC TAT GAG ACA GAA GGC AGC CGA GGG GCT    1296
Lys Pro His His Arg Ala His Tyr Glu Thr Glu Gly Ser Arg Gly Ala
            420                 425                 430

GTC AAA GCT CCA ACT GGA GGC CAC CCT GTG GTT CAG CTC CAT GGC TAC    1344
Val Lys Ala Pro Thr Gly Gly His Pro Val Val Gln Leu His Gly Tyr
        435                 440                 445

ATG GAA AAC AAG CCT CTG GGA CTT CAG ATC TTC ATT GGG ACA GCT GAT    1392
Met Glu Asn Lys Pro Leu Gly Leu Gln Ile Phe Ile Gly Thr Ala Asp
    450                 455                 460

GAG CGG ATC CTT AAG CCG CAC GCC TTC TAC CAG GTG CAC CGA ATC ACG    1440
Glu Arg Ile Leu Lys Pro His Ala Phe Tyr Gln Val His Arg Ile Thr
465                 470                 475                 480

GGG AAA ACT GTC ACC ACC ACC AGC TAT GAG AAG ATA GTG GGC AAC ACC    1488
Gly Lys Thr Val Thr Thr Thr Ser Tyr Glu Lys Ile Val Gly Asn Thr
                485                 490                 495

AAA GTC CTG GAG ATC CCC TTG GAG CCC AAA AAC AAC ATG AGG GCA ACC    1536
Lys Val Leu Glu Ile Pro Leu Glu Pro Lys Asn Asn Met Arg Ala Thr
            500                 505                 510

ATC GAC TGT GCG GGG ATC TTG AAG CTT AGA AAC GCC GAC ATT GAG CTG    1584
Ile Asp Cys Ala Gly Ile Leu Lys Leu Arg Asn Ala Asp Ile Glu Leu
        515                 520                 525

CGG AAA GGC GAG ACG GAC ATT GGA AGA AAG AAC ACG CGG GTG AGA CTG    1632
Arg Lys Gly Glu Thr Asp Ile Gly Arg Lys Asn Thr Arg Val Arg Leu
    530                 535                 540

GTT TTC CGA GTT CAC ATC CCA GAG TCC AGT GGC AGA ATC GTC TCT TTA    1680
Val Phe Arg Val His Ile Pro Glu Ser Ser Gly Arg Ile Val Ser Leu
545                 550                 555                 560

CAG ACT GCA TCT AAC CCC ATC GAG TGC TCC CAG CGA TCT GCT CAC GAG    1728
Gln Thr Ala Ser Asn Pro Ile Glu Cys Ser Gln Arg Ser Ala His Glu
                565                 570                 575

CTG CCC ATG GTT GAA AGA CAA GAC ACA GAC AGC TGC CTG GTC TAT GGC    1776
Leu Pro Met Val Glu Arg Gln Asp Thr Asp Ser Cys Leu Val Tyr Gly
            580                 585                 590

GGC CAG CAA ATG ATC CTC ACG GGG CAG AAC TTT ACA TCC GAG TCC AAA    1824
Gly Gln Gln Met Ile Leu Thr Gly Gln Asn Phe Thr Ser Glu Ser Lys
        595                 600                 605

GTT GTG TTT ACT GAG AAG ACC ACA GAT GGA CAG CAA ATT TGG GAG ATG    1872
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Val Val Phe Thr Glu Lys Thr Thr Asp Gly Gln Gln Ile Trp Glu Met
    610                 615                 620

GAA GCC ACG GTG GAT AAG GAC AAG AGC CAG CCC AAC ATG CTT TTT GTT      1920
Glu Ala Thr Val Asp Lys Asp Lys Ser Gln Pro Asn Met Leu Phe Val
625                 630                 635                 640

GAG ATC CCT GAA TAT CGG AAC AAG CAT ATC CGC ACA CCT GTA AAA GTG      1968
Glu Ile Pro Glu Tyr Arg Asn Lys His Ile Arg Thr Pro Val Lys Val
                645                 650                 655

AAC TTC TAC GTC ATC AAT GGG AAG AGA AAA CGA AGT CAG CCT CAG CAC      2016
Asn Phe Tyr Val Ile Asn Gly Lys Arg Lys Arg Ser Gln Pro Gln His
            660                 665                 670

TTT ACC TAC CAC CCA GTC CCA GCC ATC AAG ACG GAG CCC ACG GAT GAA      2064
Phe Thr Tyr His Pro Val Pro Ala Ile Lys Thr Glu Pro Thr Asp Glu
        675                 680                 685

TAT GAC CCC ACT CTG ATC TGC AGC CCC ACC CAT GGA GGC CTG GGG AGC      2112
Tyr Asp Pro Thr Leu Ile Cys Ser Pro Thr His Gly Gly Leu Gly Ser
    690                 695                 700

CAG CCT TAC TAC CCC CAG CAC CCG ATG GTG GCC GAG TCC CCC TCC TGC      2160
Gln Pro Tyr Tyr Pro Gln His Pro Met Val Ala Glu Ser Pro Ser Cys
705                 710                 715                 720

CTC GTG GCC ACC ATG GCT CCC TGC CAG CAG TTC CGC ACG GGG CTC TCA      2208
Leu Val Ala Thr Met Ala Pro Cys Gln Gln Phe Arg Thr Gly Leu Ser
                725                 730                 735

TCC CCT GAC GCC CGC TAC CAG CAA CAG AAC CCA GCG GCC GTA CTC TAC      2256
Ser Pro Asp Ala Arg Tyr Gln Gln Gln Asn Pro Ala Ala Val Leu Tyr
            740                 745                 750

CAG CGG AGC AAG AGC CTG AGC CCC AGC CTG CTG GGC TAT CAG CAG CCG      2304
Gln Arg Ser Lys Ser Leu Ser Pro Ser Leu Leu Gly Tyr Gln Gln Pro
        755                 760                 765

GCC CTC ATG GCC GCC CCG CTG TCC CTT GCG GAC GCT CAC CGC TCT GTG      2352
Ala Leu Met Ala Ala Pro Leu Ser Leu Ala Asp Ala His Arg Ser Val
    770                 775                 780

CTG GTG CAC GCC GGC TCC CAG GGC CAG AGC TCA GCC CTG CTC CAC CCC      2400
Leu Val His Ala Gly Ser Gln Gly Gln Ser Ser Ala Leu Leu His Pro
785                 790                 795                 800

TCT CCG ACC AAC CAG CAG GCC TCG CCT GTG ATC CAC TAC TCA CCC ACC      2448
Ser Pro Thr Asn Gln Gln Ala Ser Pro Val Ile His Tyr Ser Pro Thr
                805                 810                 815

AAC CAG CAG CTG CGC TGC GGA AGC CAC CAG GAG TTC CAG CAC ATC ATG      2496
Asn Gln Gln Leu Arg Cys Gly Ser His Gln Glu Phe Gln His Ile Met
            820                 825                 830

TAC TGC GAG AAT TTC GCA CCA GGC ACC ACC AGA CCT GGC CCG CCC CCG      2544
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Tyr Cys Glu Asn Phe Ala Pro Gly Thr Thr Arg Pro Gly Pro Pro Pro
        835                 840                 845

GTC AGT CAA GGT CAG AGG CTG AGC CCG GGT TCC TAC CCC ACA GTC ATT    2592
Val Ser Gln Gly Gln Arg Leu Ser Pro Gly Ser Tyr Pro Thr Val Ile
    850                 855                 860

CAG CAG CAG AAT GCC ACG AGC CAA AGA GCC GCC AAA AAC GGA CCC CCG    2640
Gln Gln Gln Asn Ala Thr Ser Gln Arg Ala Ala Lys Asn Gly Pro Pro
865                 870                 875                 880

GTC AGT GAC CAA AAG GAA GTA TTA CCT GCG GGG GTG ACC ATT AAA CAG    2688
Val Ser Asp Gln Lys Glu Val Leu Pro Ala Gly Val Thr Ile Lys Gln
                885                 890                 895

GAG CAG AAC TTG GAC CAG ACC TAC TTG GAT GAT GTT AAT GAA ATT ATC    2736
Glu Gln Asn Leu Asp Gln Thr Tyr Leu Asp Asp Val Asn Glu Ile Ile
            900                 905                 910

AGG AAG GAG TTT TCA GGA CCT CCT GCC AGA AAT CAG ACG AGA ATT CTG    2784
Arg Lys Glu Phe Ser Gly Pro Pro Ala Arg Asn Gln Thr Arg Ile Leu
        915                 920                 925

CAG TCG ACG GTA CCG CGG GCC CGG GAT CCA CCG GTC GCC ACC ATG GTG    2832
Gln Ser Thr Val Pro Arg Ala Arg Asp Pro Pro Val Ala Thr Met Val
    930                 935                 940

AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG GTC GAG    2880
Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu
945                 950                 955                 960

CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC GAG GGC    2928
Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly
                965                 970                 975

GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC TGC ACC    2976
Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr
            980                 985                 990

ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC CTG ACC    3024
Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Thr
        995                1000                1005

TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG CAG CAC    3072
Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln His
   1010                1015                1020

GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG CGC ACC    3120
Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr
1025                1030                1035                1040

ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG GTG AAG    3168
Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys
                1045                1050                1055

TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC ATC GAC    3216
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Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp
          1060                1065                1070

TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC AAC TAC    3264
Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr
      1075                1080                1085

AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC GGC ATC    3312
Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile
  1090                1095                1100

AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC GTG CAG    3360
Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val Gln
1105                1110                1115                1120

CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC CCC GTG    3408
Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val
                1125                1130                1135

CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG AGC AAA    3456
Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys
          1140                1145                1150

GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC GTG ACC    3504
Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr
      1155                1160                1165

GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TAA            3546
Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
  1170                1175                1180
```

(2) INFORMATION FOR SEQ ID NO:133:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1181 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:133:

```
Met Asn Ala Pro Glu Arg Gln Pro Gln Pro Asp Gly Gly Asp Ala Pro
 1               5                  10                  15
Gly His Glu Pro Gly Gly Ser Pro Gln Asp Glu Leu Asp Phe Ser Ile
            20                  25                  30
Leu Phe Asp Tyr Glu Tyr Leu Asn Pro Asn Glu Glu Glu Pro Asn Ala
        35                  40                  45
His Lys Val Ala Ser Pro Pro Ser Gly Pro Ala Tyr Pro Asp Asp Val
    50                  55                  60
Met Asp Tyr Gly Leu Lys Pro Tyr Ser Pro Leu Ala Ser Leu Ser Gly
65                  70                  75                  80
Glu Pro Pro Gly Arg Phe Gly Glu Pro Asp Arg Val Gly Pro Gln Lys
```

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                    85                  90                  95
Phe Leu Ser Ala Ala Lys Pro Ala Gly Ala Ser Gly Leu Ser Pro Arg
                100                 105                 110
Ile Glu Ile Thr Pro Ser His Glu Leu Ile Gln Ala Val Gly Pro Leu
        115                 120                 125
Arg Met Arg Asp Ala Gly Leu Leu Val Glu Gln Pro Pro Leu Ala Gly
    130                 135                 140
Val Ala Ala Ser Pro Arg Phe Thr Leu Pro Val Pro Gly Phe Glu Gly
145                 150                 155                 160
Tyr Arg Glu Pro Leu Cys Leu Ser Pro Ala Ser Ser Gly Ser Ser Ala
                165                 170                 175
Ser Phe Ile Ser Asp Thr Phe Ser Pro Tyr Thr Ser Pro Cys Val Ser
            180                 185                 190
Pro Asn Asn Gly Gly Pro Asp Asp Leu Cys Pro Gln Phe Gln Asn Ile
        195                 200                 205
Pro Ala His Tyr Ser Pro Arg Thr Ser Pro Ile Met Ser Pro Arg Thr
    210                 215                 220
Ser Leu Ala Glu Asp Ser Cys Leu Gly Arg His Ser Pro Val Pro Arg
225                 230                 235                 240
Pro Ala Ser Arg Ser Ser Ser Pro Gly Ala Lys Arg Arg His Ser Cys
                245                 250                 255
Ala Glu Ala Leu Val Ala Leu Pro Pro Gly Ala Ser Pro Gln Arg Ser
            260                 265                 270
Arg Ser Pro Ser Pro Gln Pro Ser Ser His Val Ala Pro Gln Asp His
        275                 280                 285
Gly Ser Pro Ala Gly Tyr Pro Pro Val Ala Gly Ser Ala Val Ile Met
    290                 295                 300
Asp Ala Leu Asn Ser Leu Ala Thr Asp Ser Pro Cys Gly Ile Pro Pro
305                 310                 315                 320
Lys Met Trp Lys Thr Ser Pro Asp Pro Ser Pro Val Ser Ala Ala Pro
                325                 330                 335
Ser Lys Ala Gly Leu Pro Arg His Ile Tyr Pro Ala Val Glu Phe Leu
            340                 345                 350
Gly Pro Cys Glu Gln Gly Glu Arg Arg Asn Ser Ala Pro Glu Ser Ile
        355                 360                 365
Leu Leu Val Pro Pro Thr Trp Pro Lys Pro Leu Val Pro Ala Ile Pro
    370                 375                 380
Ile Cys Ser Ile Pro Val Thr Ala Ser Leu Pro Pro Leu Glu Trp Pro
385                 390                 395                 400
Leu Ser Ser Gln Ser Gly Ser Tyr Glu Leu Arg Ile Glu Val Gln Pro
                405                 410                 415
Lys Pro His His Arg Ala His Tyr Glu Thr Glu Gly Ser Arg Gly Ala
            420                 425                 430
Val Lys Ala Pro Thr Gly Gly His Pro Val Val Gln Leu His Gly Tyr
        435                 440                 445
Met Glu Asn Lys Pro Leu Gly Leu Gln Ile Phe Ile Gly Thr Ala Asp
    450                 455                 460
Glu Arg Ile Leu Lys Pro His Ala Phe Tyr Gln Val His Arg Ile Thr
465                 470                 475                 480
Gly Lys Thr Val Thr Thr Thr Ser Tyr Glu Lys Ile Val Gly Asn Thr
                485                 490                 495
Lys Val Leu Glu Ile Pro Leu Glu Pro Lys Asn Asn Met Arg Ala Thr
            500                 505                 510
Ile Asp Cys Ala Gly Ile Leu Lys Leu Arg Asn Ala Asp Ile Glu Leu
        515                 520                 525
Arg Lys Gly Glu Thr Asp Ile Gly Arg Lys Asn Thr Arg Val Arg Leu
```

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    530                 535                 540
Val Phe Arg Val His Ile Pro Glu Ser Ser Gly Arg Ile Val Ser Leu
545                 550                 555                 560
Gln Thr Ala Ser Asn Pro Ile Glu Cys Ser Gln Arg Ser Ala His Glu
                565                 570                 575
Leu Pro Met Val Glu Arg Gln Asp Thr Asp Ser Cys Leu Val Tyr Gly
            580                 585                 590
Gly Gln Gln Met Ile Leu Thr Gly Gln Asn Phe Thr Ser Glu Ser Lys
        595                 600                 605
Val Val Phe Thr Glu Lys Thr Thr Asp Gly Gln Gln Ile Trp Glu Met
    610                 615                 620
Glu Ala Thr Val Asp Lys Asp Lys Ser Gln Pro Asn Met Leu Phe Val
625                 630                 635                 640
Glu Ile Pro Glu Tyr Arg Asn Lys His Ile Arg Thr Pro Val Lys Val
                645                 650                 655
Asn Phe Tyr Val Ile Asn Gly Lys Arg Lys Arg Ser Gln Pro Gln His
            660                 665                 670
Phe Thr Tyr His Pro Val Pro Ala Ile Lys Thr Glu Pro Thr Asp Glu
        675                 680                 685
Tyr Asp Pro Thr Leu Ile Cys Ser Pro Thr His Gly Gly Leu Gly Ser
    690                 695                 700
Gln Pro Tyr Tyr Pro Gln His Pro Met Val Ala Glu Ser Pro Ser Cys
705                 710                 715                 720
Leu Val Ala Thr Met Ala Pro Cys Gln Gln Phe Arg Thr Gly Leu Ser
                725                 730                 735
Ser Pro Asp Ala Arg Tyr Gln Gln Gln Asn Pro Ala Ala Val Leu Tyr
            740                 745                 750
Gln Arg Ser Lys Ser Leu Ser Pro Ser Leu Leu Gly Tyr Gln Gln Pro
        755                 760                 765
Ala Leu Met Ala Ala Pro Leu Ser Leu Ala Asp Ala His Arg Ser Val
    770                 775                 780
Leu Val His Ala Gly Ser Gln Gly Gln Ser Ser Ala Leu Leu His Pro
785                 790                 795                 800
Ser Pro Thr Asn Gln Gln Ala Ser Pro Val Ile His Tyr Ser Pro Thr
                805                 810                 815
Asn Gln Gln Leu Arg Cys Gly Ser His Gln Glu Phe Gln His Ile Met
            820                 825                 830
Tyr Cys Glu Asn Phe Ala Pro Gly Thr Thr Arg Pro Gly Pro Pro Pro
        835                 840                 845
Val Ser Gln Gly Gln Arg Leu Ser Pro Gly Ser Tyr Pro Thr Val Ile
    850                 855                 860
Gln Gln Gln Asn Ala Thr Ser Gln Arg Ala Ala Lys Asn Gly Pro Pro
865                 870                 875                 880
Val Ser Asp Gln Lys Glu Val Leu Pro Ala Gly Val Thr Ile Lys Gln
                885                 890                 895
Glu Gln Asn Leu Asp Gln Thr Tyr Leu Asp Asp Val Asn Glu Ile Ile
            900                 905                 910
Arg Lys Glu Phe Ser Gly Pro Pro Ala Arg Asn Gln Thr Arg Ile Leu
        915                 920                 925
Gln Ser Thr Val Pro Arg Ala Arg Asp Pro Pro Val Ala Thr Met Val
    930                 935                 940
Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu
945                 950                 955                 960
Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly
                965                 970                 975
Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr
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                980                 985                 990
Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Thr
        995                1000                1005
Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln His
   1010                1015                1020
Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr
025                1030                1035                1040
Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys
                1045                1050                1055
Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp
           1060                1065                1070
Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr
       1075                1080                1085
Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile
   1090                1095                1100
Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val Gln
105                1110                1115                1120
Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val
                1125                1130                1135
Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys
           1140                1145                1150
Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr
       1155                1160                1165
Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
   1170                1175                1180
```

(2) INFORMATION FOR SEQ ID NO:134:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2802 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...2799
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:134:

```
ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15

GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30

GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45

TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC     192
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Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
 50                  55                  60

CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG   240
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80

CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG   288
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95

CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG   336
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110

GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC   384
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125

ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC   432
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140

AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC   480
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160

GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC   528
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175

GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC   576
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190

CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG   624
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205

AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC   672
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220

GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC   720
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240

GGA CTC AGA TCT CGA GGG AGC ATG GGC ACC TTG CGG GAT TTA CAG TAC   768
Gly Leu Arg Ser Arg Gly Ser Met Gly Thr Leu Arg Asp Leu Gln Tyr
                245                 250                 255

GCG CTC CAG GAG AAG ATC GAG GAG CTG AGG CAG CGG GAT GCT CTC ATC   816
Ala Leu Gln Glu Lys Ile Glu Glu Leu Arg Gln Arg Asp Ala Leu Ile
            260                 265                 270

GAC GAG CTG GAG CTG GAG TTG GAT CAG AAG GAC GAA CTG ATC CAG AAG   864
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Asp Glu Leu Glu Leu Glu Leu Asp Gln Lys Asp Glu Leu Ile Gln Lys
        275                 280                 285

CTG CAG AAC GAG CTG GAC AAG TAC CGC TCG GTG ATC CGA CCA GCC ACC   912
Leu Gln Asn Glu Leu Asp Lys Tyr Arg Ser Val Ile Arg Pro Ala Thr
    290                 295                 300

CAG CAG GCG CAG AAG CAG AGC GCG AGC ACC TTG CAG GGC GAG CCG CGC   960
Gln Gln Ala Gln Lys Gln Ser Ala Ser Thr Leu Gln Gly Glu Pro Arg
305                 310                 315                 320

ACC AAG CGG CAG GCG ATC TCC GCC GAG CCC ACC GCC TTC GAC ATC CAG  1008
Thr Lys Arg Gln Ala Ile Ser Ala Glu Pro Thr Ala Phe Asp Ile Gln
                325                 330                 335

GAT CTC AGC CAT GTG ACC CTG CCC TTC TAC CCC AAG AGC CCA CAG TCC  1056
Asp Leu Ser His Val Thr Leu Pro Phe Tyr Pro Lys Ser Pro Gln Ser
            340                 345                 350

AAG GAT CTT ATA AAG GAA GCT ATC CTT GAC AAT GAC TTT ATG AAG AAC  1104
Lys Asp Leu Ile Lys Glu Ala Ile Leu Asp Asn Asp Phe Met Lys Asn
        355                 360                 365

TTG GAG CTG TCG CAG ATC CAG GAG ATT GTG GAT TGT ATG TAC CCG GTG  1152
Leu Glu Leu Ser Gln Ile Gln Glu Ile Val Asp Cys Met Tyr Pro Val
    370                 375                 380

GAG TAT GGC AAG GAC AGT TGC ATC ATC AAA GAA GGA GAC GTG GGG TCA  1200
Glu Tyr Gly Lys Asp Ser Cys Ile Ile Lys Glu Gly Asp Val Gly Ser
385                 390                 395                 400

CTG GTG TAT GTC ATG GAA GAT GGT AAG GTT GAA GTT ACA AAA GAA GGT  1248
Leu Val Tyr Val Met Glu Asp Gly Lys Val Glu Val Thr Lys Glu Gly
                405                 410                 415

GTG AAG TTG TGT ACC ATG GGT CCA GGA AAA GTG TTT GGG GAA TTG GCT  1296
Val Lys Leu Cys Thr Met Gly Pro Gly Lys Val Phe Gly Glu Leu Ala
            420                 425                 430

ATT CTT TAC AAC TGT ACC CGG ACA GCG ACC GTC AAG ACT CTT GTA AAT  1344
Ile Leu Tyr Asn Cys Thr Arg Thr Ala Thr Val Lys Thr Leu Val Asn
        435                 440                 445

GTA AAA CTC TGG GCC ATT GAT CGA CAA TGT TTT CAA ACA ATA ATG ATG  1392
Val Lys Leu Trp Ala Ile Asp Arg Gln Cys Phe Gln Thr Ile Met Met
    450                 455                 460

AGG ACA GGA CTC ATC AAG CAT ACC GAG TAT ATG GAA TTT TTA AAA AGC  1440
Arg Thr Gly Leu Ile Lys His Thr Glu Tyr Met Glu Phe Leu Lys Ser
465                 470                 475                 480

GTT CCA ACA TTC CAG AGC CTT CCT GAA GAG ATC CTC AGC AAG CTT GCT  1488
Val Pro Thr Phe Gln Ser Leu Pro Glu Glu Ile Leu Ser Lys Leu Ala
                485                 490                 495

GAT GTC CTT GAA GAG ACC CAC TAT GAA AAT GGA GAA TAT ATT ATC AGG  1536
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Asp Val Leu Glu Glu Thr His Tyr Glu Asn Gly Glu Tyr Ile Ile Arg
            500                 505                 510

CAA GGT GCA AGA GGG GAC ACC TTC TTT ATC ATC AGC AAA GGA ACG GTA    1584
Gln Gly Ala Arg Gly Asp Thr Phe Phe Ile Ile Ser Lys Gly Thr Val
        515                 520                 525

AAT GTC ACT CGT GAA GAC TCA CCG AGT GAA GAC CCA GTC TTT CTT AGA    1632
Asn Val Thr Arg Glu Asp Ser Pro Ser Glu Asp Pro Val Phe Leu Arg
    530                 535                 540

ACT TTA GGA AAA GGA GAC TGG TTT GGA GAG AAA GCC TTG CAG GGG GAA    1680
Thr Leu Gly Lys Gly Asp Trp Phe Gly Glu Lys Ala Leu Gln Gly Glu
545                 550                 555                 560

GAT GTG AGA ACA GCA AAC GTA ATT GCT GCA GAA GCT GTA ACC TGC CTT    1728
Asp Val Arg Thr Ala Asn Val Ile Ala Ala Glu Ala Val Thr Cys Leu
                565                 570                 575

GTG ATT GAC AGA GAC TCT TTT AAA CAT TTG ATT GGA GGG CTG GAT GAT    1776
Val Ile Asp Arg Asp Ser Phe Lys His Leu Ile Gly Gly Leu Asp Asp
            580                 585                 590

GTT TCT AAT AAA GCA TAT GAA GAT GCA GAA GCT AAA GCA AAA TAT GAA    1824
Val Ser Asn Lys Ala Tyr Glu Asp Ala Glu Ala Lys Ala Lys Tyr Glu
        595                 600                 605

GCT GAA GCG GCT TTC TTC GCC AAC CTG AAG CTG TCT GAT TTC AAC ATC    1872
Ala Glu Ala Ala Phe Phe Ala Asn Leu Lys Leu Ser Asp Phe Asn Ile
    610                 615                 620

ATT GAT ACC CTT GGA GTT GGA GGT TTC GGA CGA GTA GAA CTG GTC CAG    1920
Ile Asp Thr Leu Gly Val Gly Gly Phe Gly Arg Val Glu Leu Val Gln
625                 630                 635                 640

TTG AAA AGT GAA GAA TCC AAA ACG TTT GCA ATG AAG ATT CTC AAG AAA    1968
Leu Lys Ser Glu Glu Ser Lys Thr Phe Ala Met Lys Ile Leu Lys Lys
                645                 650                 655

CGT CAC ATT GTG GAC ACA AGA CAG CAG GAG CAC ATC CGC TCA GAG AAG    2016
Arg His Ile Val Asp Thr Arg Gln Gln Glu His Ile Arg Ser Glu Lys
            660                 665                 670

CAG ATC ATG CAG GGG GCT CAT TCC GAT TTC ATA GTG AGA CTG TAC AGA    2064
Gln Ile Met Gln Gly Ala His Ser Asp Phe Ile Val Arg Leu Tyr Arg
        675                 680                 685

ACA TTT AAG GAC AGC AAA TAT TTG TAT ATG TTG ATG GAA GCT TGT CTA    2112
Thr Phe Lys Asp Ser Lys Tyr Leu Tyr Met Leu Met Glu Ala Cys Leu
    690                 695                 700

GGT GGA GAG CTC TGG ACC ATT CTC AGG GAT AGA GGT TCG TTT GAA GAT    2160
Gly Gly Glu Leu Trp Thr Ile Leu Arg Asp Arg Gly Ser Phe Glu Asp
705                 710                 715                 720

TCT ACA ACC AGA TTT TAC ACA GCA TGT GTG GTA GAA GCT TTT GCC TAT    2208
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Ser Thr Thr Arg Phe Tyr Thr Ala Cys Val Val Glu Ala Phe Ala Tyr
                725                 730                 735

CTG CAT TCC AAA GGA ATC ATT TAC AGG GAC CTC AAG CCA GAA AAT CTC    2256
Leu His Ser Lys Gly Ile Ile Tyr Arg Asp Leu Lys Pro Glu Asn Leu
            740                 745                 750

ATC CTA GAT CAC CGA GGT TAT GCC AAA CTG GTT GAT TTT GGC TTT GCA    2304
Ile Leu Asp His Arg Gly Tyr Ala Lys Leu Val Asp Phe Gly Phe Ala
        755                 760                 765

AAG AAA ATA GGA TTT GGA AAG AAA ACA TGG ACT TTT TGT GGG ACT CCA    2352
Lys Lys Ile Gly Phe Gly Lys Lys Thr Trp Thr Phe Cys Gly Thr Pro
    770                 775                 780

GAG TAT GTA GCC CCA GAG ATC ATC CTG AAC AAA GGC CAT GAC ATT TCA    2400
Glu Tyr Val Ala Pro Glu Ile Ile Leu Asn Lys Gly His Asp Ile Ser
785                 790                 795                 800

GCC GAC TAC TGG TCA CTG GGA ATC CTA ATG TAT GAA CTC CTG ACT GGC    2448
Ala Asp Tyr Trp Ser Leu Gly Ile Leu Met Tyr Glu Leu Leu Thr Gly
                805                 810                 815

AGC CCA CCT TTC TCA GGC CCA GAT CCT ATG AAA ACC TAT AAC ATC ATA    2496
Ser Pro Pro Phe Ser Gly Pro Asp Pro Met Lys Thr Tyr Asn Ile Ile
            820                 825                 830

TTG AGG GGG ATT GAC ATG ATA GAA TTT CCA AAG AAG ATT GCC AAA AAT    2544
Leu Arg Gly Ile Asp Met Ile Glu Phe Pro Lys Lys Ile Ala Lys Asn
        835                 840                 845

GCT GCT AAT TTA ATT AAA AAA CTA TGC AGG GAC AAT CCA TCA GAA AGA    2592
Ala Ala Asn Leu Ile Lys Lys Leu Cys Arg Asp Asn Pro Ser Glu Arg
    850                 855                 860

TTA GGG AAT TTG AAA AAT GGA GTA AAA GAC ATT CAA AAG CAC AAA TGG    2640
Leu Gly Asn Leu Lys Asn Gly Val Lys Asp Ile Gln Lys His Lys Trp
865                 870                 875                 880

TTT GAG GGC TTT AAC TGG GAA GGC TTA AGA AAA GGT ACC TTG ACA CCT    2688
Phe Glu Gly Phe Asn Trp Glu Gly Leu Arg Lys Gly Thr Leu Thr Pro
                885                 890                 895

CCT ATA ATA CCA AGT GTT GCA TCA CCC ACA GAC ACA AGT AAT TTT GAC    2736
Pro Ile Ile Pro Ser Val Ala Ser Pro Thr Asp Thr Ser Asn Phe Asp
            900                 905                 910

AGT TTC CCT GAG GAC AAC GAT GAA CCA CCA CCT GAT GAC AAC TCA GGA    2784
Ser Phe Pro Glu Asp Asn Asp Glu Pro Pro Pro Asp Asp Asn Ser Gly
        915                 920                 925

TGG GAT ATA GAC TTC TAA                                            2802
Trp Asp Ile Asp Phe
    930
```


BNSDOCID: <WO___9845704A2_I_>

(2) INFORMATION FOR SEQ ID NO:135:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 933 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:135:

```
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240
Gly Leu Arg Ser Arg Gly Ser Met Gly Thr Leu Arg Asp Leu Gln Tyr
                245                 250                 255
Ala Leu Gln Glu Lys Ile Glu Glu Leu Arg Gln Arg Asp Ala Leu Ile
            260                 265                 270
Asp Glu Leu Glu Leu Glu Leu Asp Gln Lys Asp Glu Leu Ile Gln Lys
        275                 280                 285
Leu Gln Asn Glu Leu Asp Lys Tyr Arg Ser Val Ile Arg Pro Ala Thr
    290                 295                 300
Gln Gln Ala Gln Lys Gln Ser Ala Ser Thr Leu Gln Gly Glu Pro Arg
305                 310                 315                 320
Thr Lys Arg Gln Ala Ile Ser Ala Glu Pro Thr Ala Phe Asp Ile Gln
                325                 330                 335
Asp Leu Ser His Val Thr Leu Pro Phe Tyr Pro Lys Ser Pro Gln Ser
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340 345 350
Lys Asp Leu Ile Lys Glu Ala Ile Leu Asp Asn Asp Phe Met Lys Asn
355 360 365
Leu Glu Leu Ser Gln Ile Gln Glu Ile Val Asp Cys Met Tyr Pro Val
370 375 380
Glu Tyr Gly Lys Asp Ser Cys Ile Ile Lys Glu Gly Asp Val Gly Ser
385 390 395 400
Leu Val Tyr Val Met Glu Asp Gly Lys Val Glu Val Thr Lys Glu Gly
405 410 415
Val Lys Leu Cys Thr Met Gly Pro Gly Lys Val Phe Gly Glu Leu Ala
420 425 430
Ile Leu Tyr Asn Cys Thr Arg Thr Ala Thr Val Lys Thr Leu Val Asn
435 440 445
Val Lys Leu Trp Ala Ile Asp Arg Gln Cys Phe Gln Thr Ile Met Met
450 455 460
Arg Thr Gly Leu Ile Lys His Thr Glu Tyr Met Glu Phe Leu Lys Ser
465 470 475 480
Val Pro Thr Phe Gln Ser Leu Pro Glu Glu Ile Leu Ser Lys Leu Ala
485 490 495
Asp Val Leu Glu Glu Thr His Tyr Glu Asn Gly Glu Tyr Ile Ile Arg
500 505 510
Gln Gly Ala Arg Gly Asp Thr Phe Phe Ile Ile Ser Lys Gly Thr Val
515 520 525
Asn Val Thr Arg Glu Asp Ser Pro Ser Glu Asp Pro Val Phe Leu Arg
530 535 540
Thr Leu Gly Lys Gly Asp Trp Phe Gly Glu Lys Ala Leu Gln Gly Glu
545 550 555 560
Asp Val Arg Thr Ala Asn Val Ile Ala Ala Glu Ala Val Thr Cys Leu
565 570 575
Val Ile Asp Arg Asp Ser Phe Lys His Leu Ile Gly Gly Leu Asp Asp
580 585 590
Val Ser Asn Lys Ala Tyr Glu Asp Ala Glu Ala Lys Ala Lys Tyr Glu
595 600 605
Ala Glu Ala Ala Phe Phe Ala Asn Leu Lys Leu Ser Asp Phe Asn Ile
610 615 620
Ile Asp Thr Leu Gly Val Gly Gly Phe Gly Arg Val Glu Leu Val Gln
625 630 635 640
Leu Lys Ser Glu Glu Ser Lys Thr Phe Ala Met Lys Ile Leu Lys Lys
645 650 655
Arg His Ile Val Asp Thr Arg Gln Gln Glu His Ile Arg Ser Glu Lys
660 665 670
Gln Ile Met Gln Gly Ala His Ser Asp Phe Ile Val Arg Leu Tyr Arg
675 680 685
Thr Phe Lys Asp Ser Lys Tyr Leu Tyr Met Leu Met Glu Ala Cys Leu
690 695 700
Gly Gly Glu Leu Trp Thr Ile Leu Arg Asp Arg Gly Ser Phe Glu Asp
705 710 715 720
Ser Thr Thr Arg Phe Tyr Thr Ala Cys Val Val Glu Ala Phe Ala Tyr
725 730 735
Leu His Ser Lys Gly Ile Ile Tyr Arg Asp Leu Lys Pro Glu Asn Leu
740 745 750
Ile Leu Asp His Arg Gly Tyr Ala Lys Leu Val Asp Phe Gly Phe Ala
755 760 765
Lys Lys Ile Gly Phe Gly Lys Lys Thr Trp Thr Phe Cys Gly Thr Pro
770 775 780
Glu Tyr Val Ala Pro Glu Ile Ile Leu Asn Lys Gly His Asp Ile Ser

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785                 790                 795                 800
Ala Asp Tyr Trp Ser Leu Gly Ile Leu Met Tyr Glu Leu Leu Thr Gly
                805                 810                 815
Ser Pro Pro Phe Ser Gly Pro Asp Pro Met Lys Thr Tyr Asn Ile Ile
            820                 825                 830
Leu Arg Gly Ile Asp Met Ile Glu Phe Pro Lys Lys Ile Ala Lys Asn
        835                 840                 845
Ala Ala Asn Leu Ile Lys Lys Leu Cys Arg Asp Asn Pro Ser Glu Arg
    850                 855                 860
Leu Gly Asn Leu Lys Asn Gly Val Lys Asp Ile Gln Lys His Lys Trp
865                 870                 875                 880
Phe Glu Gly Phe Asn Trp Glu Gly Leu Arg Lys Gly Thr Leu Thr Pro
                885                 890                 895
Pro Ile Ile Pro Ser Val Ala Ser Pro Thr Asp Thr Ser Asn Phe Asp
            900                 905                 910
Ser Phe Pro Glu Asp Asn Asp Glu Pro Pro Pro Asp Asp Asn Ser Gly
        915                 920                 925
Trp Asp Ile Asp Phe
    930
```

(2) INFORMATION FOR SEQ ID NO:136:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2799 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...2795
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:136:

```
ATG GGC ACC TTG CGG GAT TTA CAG TAC GCG CTC CAG GAG AAG ATC GAG      48
Met Gly Thr Leu Arg Asp Leu Gln Tyr Ala Leu Gln Glu Lys Ile Glu
 1               5                  10                  15

GAG CTG AGG CAG CGG GAT GCT CTC ATC GAC GAG CTG GAG CTG GAG TTG      96
Glu Leu Arg Gln Arg Asp Ala Leu Ile Asp Glu Leu Glu Leu Glu Leu
            20                  25                  30

GAT CAG AAG GAC GAA CTG ATC CAG AAG CTG CAG AAC GAG CTG GAC AAG     144
Asp Gln Lys Asp Glu Leu Ile Gln Lys Leu Gln Asn Glu Leu Asp Lys
        35                  40                  45

TAC CGC TCG GTG ATC CGA CCA GCC ACC CAG CAG GCG CAG AAG CAG AGC     192
Tyr Arg Ser Val Ile Arg Pro Ala Thr Gln Gln Ala Gln Lys Gln Ser
    50                  55                  60

GCG AGC ACC TTG CAG GGC GAG CCG CGC ACC AAG CGG CAG GCG ATC TCC     240
Ala Ser Thr Leu Gln Gly Glu Pro Arg Thr Lys Arg Gln Ala Ile Ser
65                  70                  75                  80
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GCC GAG CCC ACC GCC TTC GAC ATC CAG GAT CTC AGC CAT GTG ACC CTG      288
Ala Glu Pro Thr Ala Phe Asp Ile Gln Asp Leu Ser His Val Thr Leu
                85                  90                  95

CCC TTC TAC CCC AAG AGC CCA CAG TCC AAG GAT CTT ATA AAG GAA GCT      336
Pro Phe Tyr Pro Lys Ser Pro Gln Ser Lys Asp Leu Ile Lys Glu Ala
            100                 105                 110

ATC CTT GAC AAT GAC TTT ATG AAG AAC TTG GAG CTG TCG CAG ATC CAG      384
Ile Leu Asp Asn Asp Phe Met Lys Asn Leu Glu Leu Ser Gln Ile Gln
        115                 120                 125

GAG ATT GTG GAT TGT ATG TAC CCG GTG GAG TAT GGC AAG GAC AGT TGC      432
Glu Ile Val Asp Cys Met Tyr Pro Val Glu Tyr Gly Lys Asp Ser Cys
    130                 135                 140

ATC ATC AAA GAA GGA GAC GTG GGG TCA CTG GTG TAT GTC ATG GAA GAT      480
Ile Ile Lys Glu Gly Asp Val Gly Ser Leu Val Tyr Val Met Glu Asp
145                 150                 155                 160

GGT AAG GTT GAA GTT ACA AAA GAA GGT GTG AAG TTG TGT ACC ATG GGT      528
Gly Lys Val Glu Val Thr Lys Glu Gly Val Lys Leu Cys Thr Met Gly
                165                 170                 175

CCA GGA AAA GTG TTT GGG GAA TTG GCT ATT CTT TAC AAC TGT ACC CGG      576
Pro Gly Lys Val Phe Gly Glu Leu Ala Ile Leu Tyr Asn Cys Thr Arg
            180                 185                 190

ACA GCG ACC GTC AAG ACT CTT GTA AAT GTA AAA CTC TGG GCC ATT GAT      624
Thr Ala Thr Val Lys Thr Leu Val Asn Val Lys Leu Trp Ala Ile Asp
        195                 200                 205

CGA CAA TGT TTT CAA ACA ATA ATG ATG AGG ACA GGA CTC ATC AAG CAT      672
Arg Gln Cys Phe Gln Thr Ile Met Met Arg Thr Gly Leu Ile Lys His
    210                 215                 220

ACC GAG TAT ATG GAA TTT TTA AAA AGC GTT CCA ACA TTC CAG AGC CTT      720
Thr Glu Tyr Met Glu Phe Leu Lys Ser Val Pro Thr Phe Gln Ser Leu
225                 230                 235                 240

CCT GAA GAG ATC CTC AGC AAG CTT GCT GAT GTC CTT GAA GAG ACC CAC      768
Pro Glu Glu Ile Leu Ser Lys Leu Ala Asp Val Leu Glu Glu Thr His
                245                 250                 255

TAT GAA AAT GGA GAA TAT ATT ATC AGG CAA GGT GCA AGA GGG GAC ACC      816
Tyr Glu Asn Gly Glu Tyr Ile Ile Arg Gln Gly Ala Arg Gly Asp Thr
            260                 265                 270

TTC TTT ATC ATC AGC AAA GGA ACG GTA AAT GTC ACT CGT GAA GAC TCA      864
Phe Phe Ile Ile Ser Lys Gly Thr Val Asn Val Thr Arg Glu Asp Ser
        275                 280                 285

CCG AGT GAA GAC CCA GTC TTT CTT AGA ACT TTA GGA AAA GGA GAC TGG      912
Pro Ser Glu Asp Pro Val Phe Leu Arg Thr Leu Gly Lys Gly Asp Trp
    290                 295                 300
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TTT GGA GAG AAA GCC TTG CAG GGG GAA GAT GTG AGA ACA GCA AAC GTA 960
Phe Gly Glu Lys Ala Leu Gln Gly Glu Asp Val Arg Thr Ala Asn Val
305 310 315 320

ATT GCT GCA GAA GCT GTA ACC TGC CTT GTG ATT GAC AGA GAC TCT TTT 1008
Ile Ala Ala Glu Ala Val Thr Cys Leu Val Ile Asp Arg Asp Ser Phe
325 330 335

AAA CAT TTG ATT GGA GGG CTG GAT GAT GTT TCT AAT AAA GCA TAT GAA 1056
Lys His Leu Ile Gly Gly Leu Asp Asp Val Ser Asn Lys Ala Tyr Glu
340 345 350

GAT GCA GAA GCT AAA GCA AAA TAT GAA GCT GAA GCG GCT TTC TTC GCC 1104
Asp Ala Glu Ala Lys Ala Lys Tyr Glu Ala Glu Ala Ala Phe Phe Ala
355 360 365

AAC CTG AAG CTG TCT GAT TTC AAC ATC ATT GAT ACC CTT GGA GTT GGA 1152
Asn Leu Lys Leu Ser Asp Phe Asn Ile Ile Asp Thr Leu Gly Val Gly
370 375 380

GGT TTC GGA CGA GTA GAA CTG GTC CAG TTG AAA AGT GAA GAA TCC AAA 1200
Gly Phe Gly Arg Val Glu Leu Val Gln Leu Lys Ser Glu Glu Ser Lys
385 390 395 400

ACG TTT GCA ATG AAG ATT CTC AAG AAA CGT CAC ATT GTG GAC ACA AGA 1248
Thr Phe Ala Met Lys Ile Leu Lys Lys Arg His Ile Val Asp Thr Arg
405 410 415

CAG CAG GAG CAC ATC CGC TCA GAG AAG CAG ATC ATG CAG GGG GCT CAT 1296
Gln Gln Glu His Ile Arg Ser Glu Lys Gln Ile Met Gln Gly Ala His
420 425 430

TCC GAT TTC ATA GTG AGA CTG TAC AGA ACA TTT AAG GAC AGC AAA TAT 1344
Ser Asp Phe Ile Val Arg Leu Tyr Arg Thr Phe Lys Asp Ser Lys Tyr
435 440 445

TTG TAT ATG TTG ATG GAA GCT TGT CTA GGT GGA GAG CTC TGG ACC ATT 1392
Leu Tyr Met Leu Met Glu Ala Cys Leu Gly Gly Glu Leu Trp Thr Ile
450 455 460

CTC AGG GAT AGA GGT TCG TTT GAA GAT TCT ACA ACC AGA TTT TAC ACA 1440
Leu Arg Asp Arg Gly Ser Phe Glu Asp Ser Thr Thr Arg Phe Tyr Thr
465 470 475 480

GCA TGT GTG GTA GAA GCT TTT GCC TAT CTG CAT TCC AAA GGA ATC ATT 1488
Ala Cys Val Val Glu Ala Phe Ala Tyr Leu His Ser Lys Gly Ile Ile
485 490 495

TAC AGG GAC CTC AAG CCA GAA AAT CTC ATC CTA GAT CAC CGA GGT TAT 1536
Tyr Arg Asp Leu Lys Pro Glu Asn Leu Ile Leu Asp His Arg Gly Tyr
500 505 510

GCC AAA CTG GTT GAT TTT GGC TTT GCA AAG AAA ATA GGA TTT GGA AAG 1584
Ala Lys Leu Val Asp Phe Gly Phe Ala Lys Lys Ile Gly Phe Gly Lys
515 520 525

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AAA ACA TGG ACT TTT TGT GGG ACT CCA GAG TAT GTA GCC CCA GAG ATC    1632
Lys Thr Trp Thr Phe Cys Gly Thr Pro Glu Tyr Val Ala Pro Glu Ile
    530                 535                 540

ATC CTG AAC AAA GGC CAT GAC ATT TCA GCC GAC TAC TGG TCA CTG GGA    1680
Ile Leu Asn Lys Gly His Asp Ile Ser Ala Asp Tyr Trp Ser Leu Gly
545                 550                 555                 560

ATC CTA ATG TAT GAA CTC CTG ACT GGC AGC CCA CCT TTC TCA GGC CCA    1728
Ile Leu Met Tyr Glu Leu Leu Thr Gly Ser Pro Pro Phe Ser Gly Pro
                565                 570                 575

GAT CCT ATG AAA ACC TAT AAC ATC ATA TTG AGG GGG ATT GAC ATG ATA    1776
Asp Pro Met Lys Thr Tyr Asn Ile Ile Leu Arg Gly Ile Asp Met Ile
            580                 585                 590

GAA TTT CCA AAG AAG ATT GCC AAA AAT GCT GCT AAT TTA ATT AAA AAA    1824
Glu Phe Pro Lys Lys Ile Ala Lys Asn Ala Ala Asn Leu Ile Lys Lys
        595                 600                 605

CTA TGC AGG GAC AAT CCA TCA GAA AGA TTA GGG AAT TTG AAA AAT GGA    1872
Leu Cys Arg Asp Asn Pro Ser Glu Arg Leu Gly Asn Leu Lys Asn Gly
    610                 615                 620

GTA AAA GAC ATT CAA AAG CAC AAA TGG TTT GAG GGC TTT AAC TGG GAA    1920
Val Lys Asp Ile Gln Lys His Lys Trp Phe Glu Gly Phe Asn Trp Glu
625                 630                 635                 640

GGC TTA AGA AAA GGT ACC TTG ACA CCT CCT ATA ATA CCA AGT GTT GCA    1968
Gly Leu Arg Lys Gly Thr Leu Thr Pro Pro Ile Ile Pro Ser Val Ala
                645                 650                 655

TCA CCC ACA GAC ACA AGT AAT TTT GAC AGT TTC CCT GAG GAC AAC GAT    2016
Ser Pro Thr Asp Thr Ser Asn Phe Asp Ser Phe Pro Glu Asp Asn Asp
            660                 665                 670

GAA CCA CCA CCT GAT GAC AAC TCA GGA TGG GAT ATA GAC TTC TCG GAT    2064
Glu Pro Pro Pro Asp Asp Asn Ser Gly Trp Asp Ile Asp Phe Ser Asp
        675                 680                 685

CCA CCG GTC GCC ACC ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG    2112
Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly
    690                 695                 700

GTG GTG CCC ATC CTG GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG    2160
Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys
705                 710                 715                 720

TTC AGC GTG TCC GGC GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG    2208
Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu
                725                 730                 735

ACC CTG AAG TTC ATC TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC    2256
Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro
            740                 745                 750
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ACC CTC GTG ACC ACC CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC      2304
Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr
        755                 760                 765

CCC GAC CAC ATG AAG CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA      2352
Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu
    770                 775                 780

GGC TAC GTC CAG GAG CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC      2400
Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr
785                 790                 795                 800

AAG ACC CGC GCC GAG GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC      2448
Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg
                805                 810                 815

ATC GAG CTG AAG GGC ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG      2496
Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly
            820                 825                 830

CAC AAG CTG GAG TAC AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC      2544
His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala
        835                 840                 845

GAC AAG CAG AAG AAC GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC      2592
Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn
    850                 855                 860

ATC GAG GAC GGC AGC GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC      2640
Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr
865                 870                 875                 880

CCC ATC GGC GAC GGC CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC      2688
Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser
                885                 890                 895

ACC CAG TCC GCC CTG AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG      2736
Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met
            900                 905                 910

GTC CTG CTG GAG TTC GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC      2784
Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp
        915                 920                 925

GAG CTG TAC AA GTAA                                                  2799
Glu Leu Tyr Lys
    930
```

(2) INFORMATION FOR SEQ ID NO:137:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 932 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:137:

```
Met Gly Thr Leu Arg Asp Leu Gln Tyr Ala Leu Gln Glu Lys Ile Glu
 1               5                  10                  15
Glu Leu Arg Gln Arg Asp Ala Leu Ile Asp Glu Leu Glu Leu Glu Leu
            20                  25                  30
Asp Gln Lys Asp Glu Leu Ile Gln Lys Leu Gln Asn Glu Leu Asp Lys
        35                  40                  45
Tyr Arg Ser Val Ile Arg Pro Ala Thr Gln Gln Ala Gln Lys Gln Ser
    50                  55                  60
Ala Ser Thr Leu Gln Gly Glu Pro Arg Thr Lys Arg Gln Ala Ile Ser
65                  70                  75                  80
Ala Glu Pro Thr Ala Phe Asp Ile Gln Asp Leu Ser His Val Thr Leu
                85                  90                  95
Pro Phe Tyr Pro Lys Ser Pro Gln Ser Lys Asp Leu Ile Lys Glu Ala
            100                 105                 110
Ile Leu Asp Asn Asp Phe Met Lys Asn Leu Glu Leu Ser Gln Ile Gln
        115                 120                 125
Glu Ile Val Asp Cys Met Tyr Pro Val Glu Tyr Gly Lys Asp Ser Cys
    130                 135                 140
Ile Ile Lys Glu Gly Asp Val Gly Ser Leu Val Tyr Val Met Glu Asp
145                 150                 155                 160
Gly Lys Val Glu Val Thr Lys Glu Gly Val Lys Leu Cys Thr Met Gly
                165                 170                 175
Pro Gly Lys Val Phe Gly Glu Leu Ala Ile Leu Tyr Asn Cys Thr Arg
            180                 185                 190
Thr Ala Thr Val Lys Thr Leu Val Asn Val Lys Leu Trp Ala Ile Asp
        195                 200                 205
Arg Gln Cys Phe Gln Thr Ile Met Met Arg Thr Gly Leu Ile Lys His
    210                 215                 220
Thr Glu Tyr Met Glu Phe Leu Lys Ser Val Pro Thr Phe Gln Ser Leu
225                 230                 235                 240
Pro Glu Glu Ile Leu Ser Lys Leu Ala Asp Val Leu Glu Glu Thr His
                245                 250                 255
Tyr Glu Asn Gly Glu Tyr Ile Ile Arg Gln Gly Ala Arg Gly Asp Thr
            260                 265                 270
Phe Phe Ile Ile Ser Lys Gly Thr Val Asn Val Thr Arg Glu Asp Ser
        275                 280                 285
Pro Ser Glu Asp Pro Val Phe Leu Arg Thr Leu Gly Lys Gly Asp Trp
    290                 295                 300
Phe Gly Glu Lys Ala Leu Gln Gly Glu Asp Val Arg Thr Ala Asn Val
305                 310                 315                 320
Ile Ala Ala Glu Ala Val Thr Cys Leu Val Ile Asp Arg Asp Ser Phe
                325                 330                 335
Lys His Leu Ile Gly Gly Leu Asp Asp Val Ser Asn Lys Ala Tyr Glu
            340                 345                 350
Asp Ala Glu Ala Lys Ala Lys Tyr Glu Ala Glu Ala Ala Phe Phe Ala
        355                 360                 365
Asn Leu Lys Leu Ser Asp Phe Asn Ile Ile Asp Thr Leu Gly Val Gly
    370                 375                 380
Gly Phe Gly Arg Val Glu Leu Val Gln Leu Lys Ser Glu Glu Ser Lys
```

385 390 395 400
Thr Phe Ala Met Lys Ile Leu Lys Lys Arg His Ile Val Asp Thr Arg
405 410 415
Gln Gln Glu His Ile Arg Ser Glu Lys Gln Ile Met Gln Gly Ala His
420 425 430
Ser Asp Phe Ile Val Arg Leu Tyr Arg Thr Phe Lys Asp Ser Lys Tyr
435 440 445
Leu Tyr Met Leu Met Glu Ala Cys Leu Gly Gly Glu Leu Trp Thr Ile
450 455 460
Leu Arg Asp Arg Gly Ser Phe Glu Asp Ser Thr Thr Arg Phe Tyr Thr
465 470 475 480
Ala Cys Val Val Glu Ala Phe Ala Tyr Leu His Ser Lys Gly Ile Ile
485 490 495
Tyr Arg Asp Leu Lys Pro Glu Asn Leu Ile Leu Asp His Arg Gly Tyr
500 505 510
Ala Lys Leu Val Asp Phe Gly Phe Ala Lys Lys Ile Gly Phe Gly Lys
515 520 525
Lys Thr Trp Thr Phe Cys Gly Thr Pro Glu Tyr Val Ala Pro Glu Ile
530 535 540
Ile Leu Asn Lys Gly His Asp Ile Ser Ala Asp Tyr Trp Ser Leu Gly
545 550 555 560
Ile Leu Met Tyr Glu Leu Leu Thr Gly Ser Pro Pro Phe Ser Gly Pro
565 570 575
Asp Pro Met Lys Thr Tyr Asn Ile Ile Leu Arg Gly Ile Asp Met Ile
580 585 590
Glu Phe Pro Lys Lys Ile Ala Lys Asn Ala Ala Asn Leu Ile Lys Lys
595 600 605
Leu Cys Arg Asp Asn Pro Ser Glu Arg Leu Gly Asn Leu Lys Asn Gly
610 615 620
Val Lys Asp Ile Gln Lys His Lys Trp Phe Glu Gly Phe Asn Trp Glu
625 630 635 640
Gly Leu Arg Lys Gly Thr Leu Thr Pro Pro Ile Ile Pro Ser Val Ala
645 650 655
Ser Pro Thr Asp Thr Ser Asn Phe Asp Ser Phe Pro Glu Asp Asn Asp
660 665 670
Glu Pro Pro Pro Asp Asp Asn Ser Gly Trp Asp Ile Asp Phe Ser Asp
675 680 685
Pro Pro Val Ala Thr Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly
690 695 700
Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys
705 710 715 720
Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu
725 730 735
Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro
740 745 750
Thr Leu Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr
755 760 765
Pro Asp His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu
770 775 780
Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr
785 790 795 800
Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg
805 810 815
Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly
820 825 830
His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala

```
          835                 840                 845
Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn
      850                 855                 860
Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr
865                 870                 875                 880
Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser
                885                 890                 895
Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met
            900                 905                 910
Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp
          915                 920                 925
Glu Leu Tyr Lys
      930
```

(2) INFORMATION FOR SEQ ID NO:138:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2184 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...2181
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:138:

```
ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15

GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30

GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45

TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC     192
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60

CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG     240
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80

CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG     288
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95

CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG     336
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```
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110

GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC     384
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125

ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC     432
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140

AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC     480
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160

GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC     528
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175

GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC     576
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190

CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG     624
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205

AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC     672
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220

GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC     720
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240

GGA CTC AGA TCT CGA GGC ACC ATG AGC GAC GTG GCT ATT GTG AAG GAG     768
Gly Leu Arg Ser Arg Gly Thr Met Ser Asp Val Ala Ile Val Lys Glu
                245                 250                 255

GGT TGG CTG CAC AAA CGA GGG GAG TAC ATC AAG ACC TGG CGG CCA CGC     816
Gly Trp Leu His Lys Arg Gly Glu Tyr Ile Lys Thr Trp Arg Pro Arg
            260                 265                 270

TAC TTC CTC CTC AAG AAT GAT GGC ACC TTC ATT GGC TAC AAG GAG CGG     864
Tyr Phe Leu Leu Lys Asn Asp Gly Thr Phe Ile Gly Tyr Lys Glu Arg
        275                 280                 285

CCG CAG GAT GTG GAC CAA CGT GAG GCT CCC CTC AAC AAC TTC TCT GTG     912
Pro Gln Asp Val Asp Gln Arg Glu Ala Pro Leu Asn Asn Phe Ser Val
    290                 295                 300

GCG CAG TGC CAG CTG ATG AAG ACG GAG CGG CCC CGG CCC AAC ACC TTC     960
Ala Gln Cys Gln Leu Met Lys Thr Glu Arg Pro Arg Pro Asn Thr Phe
305                 310                 315                 320

ATC ATC CGC TGC CTG CAG TGG ACC ACT GTC ATC GAA CGC ACC TTC CAT    1008
```

```
Ile Ile Arg Cys Leu Gln Trp Thr Thr Val Ile Glu Arg Thr Phe His
                325                 330                 335

GTG GAG ACT CCT GAG GAG CGG GAG GAG TGG ACA ACC GCC ATC CAG ACT    1056
Val Glu Thr Pro Glu Glu Arg Glu Glu Trp Thr Thr Ala Ile Gln Thr
            340                 345                 350

GTG GCT GAC GGC CTC AAG AAG CAG GAG GAG GAG GAG ATG GAC TTC CGG    1104
Val Ala Asp Gly Leu Lys Lys Gln Glu Glu Glu Glu Met Asp Phe Arg
        355                 360                 365

TCG GGC TCA CCC AGT GAC AAC TCA GGG GCT GAA GAG ATG GAG GTG TCC    1152
Ser Gly Ser Pro Ser Asp Asn Ser Gly Ala Glu Glu Met Glu Val Ser
    370                 375                 380

CTG GCC AAG CCC AAG CAC CGC GTG ACC ATG AAC GAG TTT GAG TAC CTG    1200
Leu Ala Lys Pro Lys His Arg Val Thr Met Asn Glu Phe Glu Tyr Leu
385                 390                 395                 400

AAG CTG CTG GGC AAG GGC ACT TTC GGC AAG GTG ATC CTG GTG AAG GAG    1248
Lys Leu Leu Gly Lys Gly Thr Phe Gly Lys Val Ile Leu Val Lys Glu
                405                 410                 415

AAG GCC ACA GGC CGC TAC TAC GCC ATG AAG ATC CTC AAG AAG GAA GTC    1296
Lys Ala Thr Gly Arg Tyr Tyr Ala Met Lys Ile Leu Lys Lys Glu Val
            420                 425                 430

ATC GTG GCC AAG GAC GAG GTG GCC CAC ACA CTC ACC GAG AAC CGC GTC    1344
Ile Val Ala Lys Asp Glu Val Ala His Thr Leu Thr Glu Asn Arg Val
        435                 440                 445

CTG CAG AAC TCC AGG CAC CCC TTC CTC ACA GCC CTG AAG TAC TCT TTC    1392
Leu Gln Asn Ser Arg His Pro Phe Leu Thr Ala Leu Lys Tyr Ser Phe
    450                 455                 460

CAG ACC CAC GAC CGC CTC TGC TTT GTC ATG GAG TAC GCC AAC GGG GGC    1440
Gln Thr His Asp Arg Leu Cys Phe Val Met Glu Tyr Ala Asn Gly Gly
465                 470                 475                 480

GAG CTG TTC TTC CAC CTG TCC CGG GAA CGT GTG TTC TCC GAG GAC CGG    1488
Glu Leu Phe Phe His Leu Ser Arg Glu Arg Val Phe Ser Glu Asp Arg
                485                 490                 495

GCC CGC TTC TAT GGC GCT GAG ATT GTG TCA GCC CTG GAC TAC CTG CAC    1536
Ala Arg Phe Tyr Gly Ala Glu Ile Val Ser Ala Leu Asp Tyr Leu His
            500                 505                 510

TCG GAG AAG AAC GTG GTG TAC CGG GAC CTC AAG CTG GAG AAC CTC ATG    1584
Ser Glu Lys Asn Val Val Tyr Arg Asp Leu Lys Leu Glu Asn Leu Met
        515                 520                 525

CTG GAC AAG GAC GGG CAC ATT AAG ATC ACA GAC TTC GGG CTG TGC AAG    1632
Leu Asp Lys Asp Gly His Ile Lys Ile Thr Asp Phe Gly Leu Cys Lys
    530                 535                 540

GAG GGG ATC AAG GAC GGT GCC ACC ATG AAG ACC TTT TGC GGC ACA CCT    1680
```

```
Glu Gly Ile Lys Asp Gly Ala Thr Met Lys Thr Phe Cys Gly Thr Pro
545                 550                 555                 560

GAG TAC CTG GCC CCC GAG GTG CTG GAG GAC AAT GAC TAC GGC CGT GCA    1728
Glu Tyr Leu Ala Pro Glu Val Leu Glu Asp Asn Asp Tyr Gly Arg Ala
                565                 570                 575

GTG GAC TGG TGG GGG CTG GGC GTG GTC ATG TAC GAG ATG ATG TGC GGT    1776
Val Asp Trp Trp Gly Leu Gly Val Val Met Tyr Glu Met Met Cys Gly
            580                 585                 590

CGC CTG CCC TTC TAC AAC CAG GAC CAT GAG AAG CTT TTT GAG CTC ATC    1824
Arg Leu Pro Phe Tyr Asn Gln Asp His Glu Lys Leu Phe Glu Leu Ile
        595                 600                 605

CTC ATG GAG GAG ATC CGC TTC CCG CGC ACG CTT GGT CCC GAG GCC AAG    1872
Leu Met Glu Glu Ile Arg Phe Pro Arg Thr Leu Gly Pro Glu Ala Lys
    610                 615                 620

TCC TTG CTT TCA GGG CTG CTC AAG AAG GAC CCC AAG CAG AGG CTT GGC    1920
Ser Leu Leu Ser Gly Leu Leu Lys Lys Asp Pro Lys Gln Arg Leu Gly
625                 630                 635                 640

GGG GGC TCC GAG GAC GCC AAG GAG ATC ATG CAG CAT CGC TTC TTT GCC    1968
Gly Gly Ser Glu Asp Ala Lys Glu Ile Met Gln His Arg Phe Phe Ala
                645                 650                 655

GGT ATC GTG TGG CAG CAC GTG TAC GAG AAG AAG CTC AGC CCA CCC TTC    2016
Gly Ile Val Trp Gln His Val Tyr Glu Lys Lys Leu Ser Pro Pro Phe
            660                 665                 670

AAG CCC CAG GTC ACG TCG GAG ACT GAC ACC AGG TAT TTT GAT GAG GAG    2064
Lys Pro Gln Val Thr Ser Glu Thr Asp Thr Arg Tyr Phe Asp Glu Glu
        675                 680                 685

TTC ACG GCC CAG ATG ATC ACC ATC ACA CCA CCT GAC CAA GAT GAC AGC    2112
Phe Thr Ala Gln Met Ile Thr Ile Thr Pro Pro Asp Gln Asp Asp Ser
    690                 695                 700

ATG GAG TGT GTG GAC AGC GAG CGC AGG CCC CAC TTC CCC CAG TTC TCC    2160
Met Glu Cys Val Asp Ser Glu Arg Arg Pro His Phe Pro Gln Phe Ser
705                 710                 715                 720

TAC TCG GCC AGC AGC ACG GCC TGA                                    2184
Tyr Ser Ala Ser Ser Thr Ala
                725
```

(2) INFORMATION FOR SEQ ID NO:139:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 727 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:139:

```
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240
Gly Leu Arg Ser Arg Gly Thr Met Ser Asp Val Ala Ile Val Lys Glu
                245                 250                 255
Gly Trp Leu His Lys Arg Gly Glu Tyr Ile Lys Thr Trp Arg Pro Arg
            260                 265                 270
Tyr Phe Leu Leu Lys Asn Asp Gly Thr Phe Ile Gly Tyr Lys Glu Arg
        275                 280                 285
Pro Gln Asp Val Asp Gln Arg Glu Ala Pro Leu Asn Asn Phe Ser Val
    290                 295                 300
Ala Gln Cys Gln Leu Met Lys Thr Glu Arg Pro Arg Pro Asn Thr Phe
305                 310                 315                 320
Ile Ile Arg Cys Leu Gln Trp Thr Thr Val Ile Glu Arg Thr Phe His
                325                 330                 335
Val Glu Thr Pro Glu Glu Arg Glu Glu Trp Thr Thr Ala Ile Gln Thr
            340                 345                 350
Val Ala Asp Gly Leu Lys Lys Gln Glu Glu Glu Glu Met Asp Phe Arg
        355                 360                 365
Ser Gly Ser Pro Ser Asp Asn Ser Gly Ala Glu Glu Met Glu Val Ser
    370                 375                 380
Leu Ala Lys Pro Lys His Arg Val Thr Met Asn Glu Phe Glu Tyr Leu
385                 390                 395                 400
Lys Leu Leu Gly Lys Gly Thr Phe Gly Lys Val Ile Leu Val Lys Glu
```


BNSDOCID: <WO__9845704A2_I_>

```
                405                 410                 415
Lys Ala Thr Gly Arg Tyr Tyr Ala Met Lys Ile Leu Lys Lys Glu Val
            420                 425                 430
Ile Val Ala Lys Asp Glu Val Ala His Thr Leu Thr Glu Asn Arg Val
        435                 440                 445
Leu Gln Asn Ser Arg His Pro Phe Leu Thr Ala Leu Lys Tyr Ser Phe
    450                 455                 460
Gln Thr His Asp Arg Leu Cys Phe Val Met Glu Tyr Ala Asn Gly Gly
465                 470                 475                 480
Glu Leu Phe Phe His Leu Ser Arg Glu Arg Val Phe Ser Glu Asp Arg
                485                 490                 495
Ala Arg Phe Tyr Gly Ala Glu Ile Val Ser Ala Leu Asp Tyr Leu His
            500                 505                 510
Ser Glu Lys Asn Val Val Tyr Arg Asp Leu Lys Leu Glu Asn Leu Met
        515                 520                 525
Leu Asp Lys Asp Gly His Ile Lys Ile Thr Asp Phe Gly Leu Cys Lys
    530                 535                 540
Glu Gly Ile Lys Asp Gly Ala Thr Met Lys Thr Phe Cys Gly Thr Pro
545                 550                 555                 560
Glu Tyr Leu Ala Pro Glu Val Leu Glu Asp Asn Asp Tyr Gly Arg Ala
                565                 570                 575
Val Asp Trp Trp Gly Leu Gly Val Val Met Tyr Glu Met Met Cys Gly
            580                 585                 590
Arg Leu Pro Phe Tyr Asn Gln Asp His Glu Lys Leu Phe Glu Leu Ile
        595                 600                 605
Leu Met Glu Glu Ile Arg Phe Pro Arg Thr Leu Gly Pro Glu Ala Lys
    610                 615                 620
Ser Leu Leu Ser Gly Leu Leu Lys Lys Asp Pro Lys Gln Arg Leu Gly
625                 630                 635                 640
Gly Gly Ser Glu Asp Ala Lys Glu Ile Met Gln His Arg Phe Phe Ala
                645                 650                 655
Gly Ile Val Trp Gln His Val Tyr Glu Lys Lys Leu Ser Pro Pro Phe
            660                 665                 670
Lys Pro Gln Val Thr Ser Glu Thr Asp Thr Arg Tyr Phe Asp Glu Glu
        675                 680                 685
Phe Thr Ala Gln Met Ile Thr Ile Thr Pro Pro Asp Gln Asp Asp Ser
    690                 695                 700
Met Glu Cys Val Asp Ser Glu Arg Arg Pro His Phe Pro Gln Phe Ser
705                 710                 715                 720
Tyr Ser Ala Ser Ser Thr Ala
                725
```

(2) INFORMATION FOR SEQ ID NO:140:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2394 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...2391
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:140:

```
ATG GAC GAA CTG TTC CCC CTC ATC TTC CCG GCA GAG CCA GCC CAG GCC      48
Met Asp Glu Leu Phe Pro Leu Ile Phe Pro Ala Glu Pro Ala Gln Ala
 1               5                  10                  15

TCT GGC CCC TAT GTG GAG ATC ATT GAG CAG CCC AAG CAG CGG GGC ATG      96
Ser Gly Pro Tyr Val Glu Ile Ile Glu Gln Pro Lys Gln Arg Gly Met
            20                  25                  30

CGC TTC CGC TAC AAG TGC GAG GGG CGC TCC GCG GGC AGC ATC CCA GGC     144
Arg Phe Arg Tyr Lys Cys Glu Gly Arg Ser Ala Gly Ser Ile Pro Gly
        35                  40                  45

GAG AGG AGC ACA GAT ACC ACC AAG ACC CAC CCC ACC ATC AAG ATC AAT     192
Glu Arg Ser Thr Asp Thr Thr Lys Thr His Pro Thr Ile Lys Ile Asn
    50                  55                  60

GGC TAC ACA GGA CCA GGG ACA GTG CGC ATC TCC CTG GTC ACC AAG GAC     240
Gly Tyr Thr Gly Pro Gly Thr Val Arg Ile Ser Leu Val Thr Lys Asp
65                  70                  75                  80

CCT CCT CAC CGG CCT CAC CCC CAC GAG CTT GTA GGA AAG GAC TGC CGG     288
Pro Pro His Arg Pro His Pro His Glu Leu Val Gly Lys Asp Cys Arg
                85                  90                  95

GAT GGC TTC TAT GAG GCT GAG CTC TGC CCG GAC CGC TGC ATC CAC AGT     336
Asp Gly Phe Tyr Glu Ala Glu Leu Cys Pro Asp Arg Cys Ile His Ser
            100                 105                 110

TTC CAG AAC CTG GGA ATC CAG TGT GTG AAG AAG CGG GAC CTG GAG CAG     384
Phe Gln Asn Leu Gly Ile Gln Cys Val Lys Lys Arg Asp Leu Glu Gln
        115                 120                 125

GCT ATC AGT CAG CGC ATC CAG ACC AAC AAC AAC CCC TTC CAA GTT CCT     432
Ala Ile Ser Gln Arg Ile Gln Thr Asn Asn Asn Pro Phe Gln Val Pro
    130                 135                 140

ATA GAA GAG CAG CGT GGG GAC TAC GAC CTG AAT GCT GTG CGG CTC TGC     480
Ile Glu Glu Gln Arg Gly Asp Tyr Asp Leu Asn Ala Val Arg Leu Cys
145                 150                 155                 160

TTC CAG GTG ACA GTG CGG GAC CCA TCA GGC AGG CCC CTC CGC CTG CCG     528
Phe Gln Val Thr Val Arg Asp Pro Ser Gly Arg Pro Leu Arg Leu Pro
                165                 170                 175

CCT GTC CTT CCT CAT CCC ATC TTT GAC AAT CGT GCC CCC AAC ACT GCC     576
Pro Val Leu Pro His Pro Ile Phe Asp Asn Arg Ala Pro Asn Thr Ala
            180                 185                 190

GAG CTC AAG ATC TGC CGA GTG AAC CGA AAC TCT GGC AGC TGC CTC GGT     624
Glu Leu Lys Ile Cys Arg Val Asn Arg Asn Ser Gly Ser Cys Leu Gly
        195                 200                 205

GGG GAT GAG ATC TTC CTA CTG TGT GAC AAG GTG CAG AAA GAG GAC ATT     672
```

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Gly Asp Glu Ile Phe Leu Leu Cys Asp Lys Val Gln Lys Glu Asp Ile
    210                 215                 220

GAG GTG TAT TTC ACG GGA CCA GGC TGG GAG GCC CGA GGC TCC TTT TCG      720
Glu Val Tyr Phe Thr Gly Pro Gly Trp Glu Ala Arg Gly Ser Phe Ser
225                 230                 235                 240

CAA GCT GAT GTG CAC CGA CAA GTG GCC ATT GTG TTC CGG ACC CCT CCC      768
Gln Ala Asp Val His Arg Gln Val Ala Ile Val Phe Arg Thr Pro Pro
                245                 250                 255

TAC GCA GAC CCC AGC CTG CAG GCT CCT GTG CGT GTC TCC ATG CAG CTG      816
Tyr Ala Asp Pro Ser Leu Gln Ala Pro Val Arg Val Ser Met Gln Leu
            260                 265                 270

CGG CGG CCT TCC GAC CGG GAG CTC AGT GAG CCC ATG GAA TTC CAG TAC      864
Arg Arg Pro Ser Asp Arg Glu Leu Ser Glu Pro Met Glu Phe Gln Tyr
        275                 280                 285

CTG CCA GAT ACA GAC GAT CGT CAC CGG ATT GAG GAG AAA CGT AAA AGG      912
Leu Pro Asp Thr Asp Asp Arg His Arg Ile Glu Glu Lys Arg Lys Arg
    290                 295                 300

ACA TAT GAG ACC TTC AAG AGC ATC ATG AAG AAG AGT CCT TTC AGC GGA      960
Thr Tyr Glu Thr Phe Lys Ser Ile Met Lys Lys Ser Pro Phe Ser Gly
305                 310                 315                 320

CCC ACC GAC CCC CGG CCT CCA CCT CGA CGC ATT GCT GTG CCT TCC CGC     1008
Pro Thr Asp Pro Arg Pro Pro Pro Arg Arg Ile Ala Val Pro Ser Arg
                325                 330                 335

AGC TCA GCT TCT GTC CCC AAG CCA GCA CCC CAG CCC TAT CCC TTT ACG     1056
Ser Ser Ala Ser Val Pro Lys Pro Ala Pro Gln Pro Tyr Pro Phe Thr
            340                 345                 350

TCA TCC CTG AGC ACC ATC AAC TAT GAT GAG TTT CCC ACC ATG GTG TTT     1104
Ser Ser Leu Ser Thr Ile Asn Tyr Asp Glu Phe Pro Thr Met Val Phe
        355                 360                 365

CCT TCT GGG CAG ATC AGC CAG GCC TCG GCC TTG GCC CCG GCC CCT CCC     1152
Pro Ser Gly Gln Ile Ser Gln Ala Ser Ala Leu Ala Pro Ala Pro Pro
    370                 375                 380

CAA GTC CTG CCC CAG GCT CCA GCC CCT GCC CCT GCT CCA GCC ATG GTA     1200
Gln Val Leu Pro Gln Ala Pro Ala Pro Ala Pro Ala Pro Ala Met Val
385                 390                 395                 400

TCA GCT CTG GCC CAG GCC CCA GCC CCT GTC CCA GTC CTA GCC CCA GGC     1248
Ser Ala Leu Ala Gln Ala Pro Ala Pro Val Pro Val Leu Ala Pro Gly
                405                 410                 415

CCT CCT CAG GCT GTG GCC CCA CCT GCC CCC AAG CCC ACC CAG GCT GGG     1296
Pro Pro Gln Ala Val Ala Pro Pro Ala Pro Lys Pro Thr Gln Ala Gly
            420                 425                 430

GAA GGA ACG CTG TCA GAG GCC CTG CTG CAG CTG CAG TTT GAT GAT GAA     1344
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```
Glu Gly Thr Leu Ser Glu Ala Leu Leu Gln Leu Gln Phe Asp Asp Glu
        435                 440                 445

GAC CTG GGG GCC TTG CTT GGC AAC AGC ACA GAC CCA GCT GTG TTC ACA    1392
Asp Leu Gly Ala Leu Leu Gly Asn Ser Thr Asp Pro Ala Val Phe Thr
    450                 455                 460

GAC CTG GCA TCC GTC GAC AAC TCC GAG TTT CAG CAG CTG CTG AAC CAG    1440
Asp Leu Ala Ser Val Asp Asn Ser Glu Phe Gln Gln Leu Leu Asn Gln
465                 470                 475                 480

GGC ATA CCT GTG GCC CCC CAC ACA ACT GAG CCC ATG CTG ATG GAG TAC    1488
Gly Ile Pro Val Ala Pro His Thr Thr Glu Pro Met Leu Met Glu Tyr
                485                 490                 495

CCT GAG GCT ATA ACT CGC CTA GTG ACA GGG GCC CAG AGG CCC CCC GAC    1536
Pro Glu Ala Ile Thr Arg Leu Val Thr Gly Ala Gln Arg Pro Pro Asp
            500                 505                 510

CCA GCT CCT GCT CCA CTG GGG GCC CCG GGG CTC CCC AAT GGC CTC CTT    1584
Pro Ala Pro Ala Pro Leu Gly Ala Pro Gly Leu Pro Asn Gly Leu Leu
        515                 520                 525

TCA GGA GAT GAA GAC TTC TCC TCC ATT GCG GAC ATG GAC TTC TCA GCC    1632
Ser Gly Asp Glu Asp Phe Ser Ser Ile Ala Asp Met Asp Phe Ser Ala
    530                 535                 540

CTG CTG AGT CAG ATC AGC TCC TTG GAT CCA CCG GTC GCC ACC ATG GTG    1680
Leu Leu Ser Gln Ile Ser Ser Leu Asp Pro Pro Val Ala Thr Met Val
545                 550                 555                 560

AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG GTC GAG    1728
Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu
                565                 570                 575

CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC GAG GGC    1776
Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly
            580                 585                 590

GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC TGC ACC    1824
Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr
        595                 600                 605

ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC CTG ACC    1872
Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Thr
    610                 615                 620

TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG CAG CAC    1920
Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln His
625                 630                 635                 640

GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG CGC ACC    1968
Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr
                645                 650                 655

ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG GTG AAG    2016
```


BNSDOCID: <WO___9845704A2_I_>

```
Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys
            660                 665                 670

TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC ATC GAC    2064
Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp
        675                 680                 685

TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC AAC TAC    2112
Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr
    690                 695                 700

AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC GGC ATC    2160
Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile
705                 710                 715                 720

AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC GTG CAG    2208
Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val Gln
                725                 730                 735

CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC CCC GTG    2256
Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val
            740                 745                 750

CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG AGC AAA    2304
Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys
        755                 760                 765

GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC GTG ACC    2352
Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr
    770                 775                 780

GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TAA            2394
Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
785                 790                 795
```

(2) INFORMATION FOR SEQ ID NO:141:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 797 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:141:

```
Met Asp Glu Leu Phe Pro Leu Ile Phe Pro Ala Glu Pro Ala Gln Ala
 1               5                  10                  15
Ser Gly Pro Tyr Val Glu Ile Ile Glu Gln Pro Lys Gln Arg Gly Met
            20                  25                  30
Arg Phe Arg Tyr Lys Cys Glu Gly Arg Ser Ala Gly Ser Ile Pro Gly
        35                  40                  45
Glu Arg Ser Thr Asp Thr Thr Lys Thr His Pro Thr Ile Lys Ile Asn
```

```
    50                  55                  60
Gly Tyr Thr Gly Pro Gly Thr Val Arg Ile Ser Leu Val Thr Lys Asp
65                  70                  75                  80
Pro Pro His Arg Pro His Pro His Glu Leu Val Gly Lys Asp Cys Arg
                85                  90                  95
Asp Gly Phe Tyr Glu Ala Glu Leu Cys Pro Asp Arg Cys Ile His Ser
            100                 105                 110
Phe Gln Asn Leu Gly Ile Gln Cys Val Lys Lys Arg Asp Leu Glu Gln
        115                 120                 125
Ala Ile Ser Gln Arg Ile Gln Thr Asn Asn Asn Pro Phe Gln Val Pro
    130                 135                 140
Ile Glu Glu Gln Arg Gly Asp Tyr Asp Leu Asn Ala Val Arg Leu Cys
145                 150                 155                 160
Phe Gln Val Thr Val Arg Asp Pro Ser Gly Arg Pro Leu Arg Leu Pro
                165                 170                 175
Pro Val Leu Pro His Pro Ile Phe Asp Asn Arg Ala Pro Asn Thr Ala
            180                 185                 190
Glu Leu Lys Ile Cys Arg Val Asn Arg Asn Ser Gly Ser Cys Leu Gly
        195                 200                 205
Gly Asp Glu Ile Phe Leu Leu Cys Asp Lys Val Gln Lys Glu Asp Ile
    210                 215                 220
Glu Val Tyr Phe Thr Gly Pro Gly Trp Glu Ala Arg Gly Ser Phe Ser
225                 230                 235                 240
Gln Ala Asp Val His Arg Gln Val Ala Ile Val Phe Arg Thr Pro Pro
                245                 250                 255
Tyr Ala Asp Pro Ser Leu Gln Ala Pro Val Arg Val Ser Met Gln Leu
            260                 265                 270
Arg Arg Pro Ser Asp Arg Glu Leu Ser Glu Pro Met Glu Phe Gln Tyr
        275                 280                 285
Leu Pro Asp Thr Asp Asp Arg His Arg Ile Glu Glu Lys Arg Lys Arg
    290                 295                 300
Thr Tyr Glu Thr Phe Lys Ser Ile Met Lys Lys Ser Pro Phe Ser Gly
305                 310                 315                 320
Pro Thr Asp Pro Arg Pro Pro Pro Arg Arg Ile Ala Val Pro Ser Arg
                325                 330                 335
Ser Ser Ala Ser Val Pro Lys Pro Ala Pro Gln Pro Tyr Pro Phe Thr
            340                 345                 350
Ser Ser Leu Ser Thr Ile Asn Tyr Asp Glu Phe Pro Thr Met Val Phe
        355                 360                 365
Pro Ser Gly Gln Ile Ser Gln Ala Ser Ala Leu Ala Pro Ala Pro Pro
    370                 375                 380
Gln Val Leu Pro Gln Ala Pro Ala Pro Ala Pro Ala Pro Ala Met Val
385                 390                 395                 400
Ser Ala Leu Ala Gln Ala Pro Ala Pro Val Pro Val Leu Ala Pro Gly
                405                 410                 415
Pro Pro Gln Ala Val Ala Pro Pro Ala Pro Lys Pro Thr Gln Ala Gly
            420                 425                 430
Glu Gly Thr Leu Ser Glu Ala Leu Leu Gln Leu Gln Phe Asp Asp Glu
        435                 440                 445
Asp Leu Gly Ala Leu Leu Gly Asn Ser Thr Asp Pro Ala Val Phe Thr
    450                 455                 460
Asp Leu Ala Ser Val Asp Asn Ser Glu Phe Gln Gln Leu Leu Asn Gln
465                 470                 475                 480
Gly Ile Pro Val Ala Pro His Thr Thr Glu Pro Met Leu Met Glu Tyr
                485                 490                 495
Pro Glu Ala Ile Thr Arg Leu Val Thr Gly Ala Gln Arg Pro Pro Asp
```

```
                500                 505                 510
Pro Ala Pro Ala Pro Leu Gly Ala Pro Gly Leu Pro Asn Gly Leu Leu
        515                 520                 525
Ser Gly Asp Glu Asp Phe Ser Ser Ile Ala Asp Met Asp Phe Ser Ala
    530                 535                 540
Leu Leu Ser Gln Ile Ser Ser Leu Asp Pro Pro Val Ala Thr Met Val
545                 550                 555                 560
Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu
                565                 570                 575
Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly
            580                 585                 590
Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr
        595                 600                 605
Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Thr
    610                 615                 620
Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Gln His
625                 630                 635                 640
Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr
                645                 650                 655
Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys
            660                 665                 670
Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp
        675                 680                 685
Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr
    690                 695                 700
Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile
705                 710                 715                 720
Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val Gln
                725                 730                 735
Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val
            740                 745                 750
Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys
        755                 760                 765
Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr
    770                 775                 780
Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
785                 790                 795
```

(2) INFORMATION FOR SEQ ID NO:142:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2394 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA
(ix) FEATURE:

(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...2391
(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:142:

```
ATG GTG AGC AAG GGC GAG GAG CTG TTC ACC GGG GTG GTG CCC ATC CTG      48
```

```
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15

GTC GAG CTG GAC GGC GAC GTA AAC GGC CAC AAG TTC AGC GTG TCC GGC      96
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30

GAG GGC GAG GGC GAT GCC ACC TAC GGC AAG CTG ACC CTG AAG TTC ATC     144
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45

TGC ACC ACC GGC AAG CTG CCC GTG CCC TGG CCC ACC CTC GTG ACC ACC     192
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60

CTG ACC TAC GGC GTG CAG TGC TTC AGC CGC TAC CCC GAC CAC ATG AAG     240
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80

CAG CAC GAC TTC TTC AAG TCC GCC ATG CCC GAA GGC TAC GTC CAG GAG     288
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
                85                  90                  95

CGC ACC ATC TTC TTC AAG GAC GAC GGC AAC TAC AAG ACC CGC GCC GAG     336
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110

GTG AAG TTC GAG GGC GAC ACC CTG GTG AAC CGC ATC GAG CTG AAG GGC     384
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125

ATC GAC TTC AAG GAG GAC GGC AAC ATC CTG GGG CAC AAG CTG GAG TAC     432
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140

AAC TAC AAC AGC CAC AAC GTC TAT ATC ATG GCC GAC AAG CAG AAG AAC     480
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160

GGC ATC AAG GTG AAC TTC AAG ATC CGC CAC AAC ATC GAG GAC GGC AGC     528
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175

GTG CAG CTC GCC GAC CAC TAC CAG CAG AAC ACC CCC ATC GGC GAC GGC     576
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190

CCC GTG CTG CTG CCC GAC AAC CAC TAC CTG AGC ACC CAG TCC GCC CTG     624
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205

AGC AAA GAC CCC AAC GAG AAG CGC GAT CAC ATG GTC CTG CTG GAG TTC     672
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220

GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC     720
```


BNSDOCID: <WO___9845704A2_I_>

```
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240

GGA CTC AGA TCT CGA GCC ATG GAC GAA CTG TTC CCC CTC ATC TTC CCG     768
Gly Leu Arg Ser Arg Ala Met Asp Glu Leu Phe Pro Leu Ile Phe Pro
                245                 250                 255

GCA GAG CCA GCC CAG GCC TCT GGC CCC TAT GTG GAG ATC ATT GAG CAG     816
Ala Glu Pro Ala Gln Ala Ser Gly Pro Tyr Val Glu Ile Ile Glu Gln
            260                 265                 270

CCC AAG CAG CGG GGC ATG CGC TTC CGC TAC AAG TGC GAG GGG CGC TCC     864
Pro Lys Gln Arg Gly Met Arg Phe Arg Tyr Lys Cys Glu Gly Arg Ser
        275                 280                 285

GCG GGC AGC ATC CCA GGC GAG AGG AGC ACA GAT ACC ACC AAG ACC CAC     912
Ala Gly Ser Ile Pro Gly Glu Arg Ser Thr Asp Thr Thr Lys Thr His
    290                 295                 300

CCC ACC ATC AAG ATC AAT GGC TAC ACA GGA CCA GGG ACA GTG CGC ATC     960
Pro Thr Ile Lys Ile Asn Gly Tyr Thr Gly Pro Gly Thr Val Arg Ile
305                 310                 315                 320

TCC CTG GTC ACC AAG GAC CCT CCT CAC CGG CCT CAC CCC CAC GAG CTT    1008
Ser Leu Val Thr Lys Asp Pro Pro His Arg Pro His Pro His Glu Leu
                325                 330                 335

GTA GGA AAG GAC TGC CGG GAT GGC TTC TAT GAG GCT GAG CTC TGC CCG    1056
Val Gly Lys Asp Cys Arg Asp Gly Phe Tyr Glu Ala Glu Leu Cys Pro
            340                 345                 350

GAC CGC TGC ATC CAC AGT TTC CAG AAC CTG GGA ATC CAG TGT GTG AAG    1104
Asp Arg Cys Ile His Ser Phe Gln Asn Leu Gly Ile Gln Cys Val Lys
        355                 360                 365

AAG CGG GAC CTG GAG CAG GCT ATC AGT CAG CGC ATC CAG ACC AAC AAC    1152
Lys Arg Asp Leu Glu Gln Ala Ile Ser Gln Arg Ile Gln Thr Asn Asn
    370                 375                 380

AAC CCC TTC CAA GTT CCT ATA GAA GAG CAG CGT GGG GAC TAC GAC CTG    1200
Asn Pro Phe Gln Val Pro Ile Glu Glu Gln Arg Gly Asp Tyr Asp Leu
385                 390                 395                 400

AAT GCT GTG CGG CTC TGC TTC CAG GTG ACA GTG CGG GAC CCA TCA GGC    1248
Asn Ala Val Arg Leu Cys Phe Gln Val Thr Val Arg Asp Pro Ser Gly
                405                 410                 415

AGG CCC CTC CGC CTG CCG CCT GTC CTT CCT CAT CCC ATC TTT GAC AAT    1296
Arg Pro Leu Arg Leu Pro Pro Val Leu Pro His Pro Ile Phe Asp Asn
            420                 425                 430

CGT GCC CCC AAC ACT GCC GAG CTC AAG ATC TGC CGA GTG AAC CGA AAC    1344
Arg Ala Pro Asn Thr Ala Glu Leu Lys Ile Cys Arg Val Asn Arg Asn
        435                 440                 445

TCT GGC AGC TGC CTC GGT GGG GAT GAG ATC TTC CTA CTG TGT GAC AAG    1392
```

```
Ser Gly Ser Cys Leu Gly Gly Asp Glu Ile Phe Leu Leu Cys Asp Lys
    450                 455                 460

GTG CAG AAA GAG GAC ATT GAG GTG TAT TTC ACG GGA CCA GGC TGG GAG    1440
Val Gln Lys Glu Asp Ile Glu Val Tyr Phe Thr Gly Pro Gly Trp Glu
465                 470                 475                 480

GCC CGA GGC TCC TTT TCG CAA GCT GAT GTG CAC CGA CAA GTG GCC ATT    1488
Ala Arg Gly Ser Phe Ser Gln Ala Asp Val His Arg Gln Val Ala Ile
                485                 490                 495

GTG TTC CGG ACC CCT CCC TAC GCA GAC CCC AGC CTG CAG GCT CCT GTG    1536
Val Phe Arg Thr Pro Pro Tyr Ala Asp Pro Ser Leu Gln Ala Pro Val
            500                 505                 510

CGT GTC TCC ATG CAG CTG CGG CGG CCT TCC GAC CGG GAG CTC AGT GAG    1584
Arg Val Ser Met Gln Leu Arg Arg Pro Ser Asp Arg Glu Leu Ser Glu
        515                 520                 525

CCC ATG GAA TTC CAG TAC CTG CCA GAT ACA GAC GAT CGT CAC CGG ATT    1632
Pro Met Glu Phe Gln Tyr Leu Pro Asp Thr Asp Asp Arg His Arg Ile
    530                 535                 540

GAG GAG AAA CGT AAA AGG ACA TAT GAG ACC TTC AAG AGC ATC ATG AAG    1680
Glu Glu Lys Arg Lys Arg Thr Tyr Glu Thr Phe Lys Ser Ile Met Lys
545                 550                 555                 560

AAG AGT CCT TTC AGC GGA CCC ACC GAC CCC CGG CCT CCA CCT CGA CGC    1728
Lys Ser Pro Phe Ser Gly Pro Thr Asp Pro Arg Pro Pro Pro Arg Arg
                565                 570                 575

ATT GCT GTG CCT TCC CGC AGC TCA GCT TCT GTC CCC AAG CCA GCA CCC    1776
Ile Ala Val Pro Ser Arg Ser Ser Ala Ser Val Pro Lys Pro Ala Pro
            580                 585                 590

CAG CCC TAT CCC TTT ACG TCA TCC CTG AGC ACC ATC AAC TAT GAT GAG    1824
Gln Pro Tyr Pro Phe Thr Ser Ser Leu Ser Thr Ile Asn Tyr Asp Glu
        595                 600                 605

TTT CCC ACC ATG GTG TTT CCT TCT GGG CAG ATC AGC CAG GCC TCG GCC    1872
Phe Pro Thr Met Val Phe Pro Ser Gly Gln Ile Ser Gln Ala Ser Ala
    610                 615                 620

TTG GCC CCG GCC CCT CCC CAA GTC CTG CCC CAG GCT CCA GCC CCT GCC    1920
Leu Ala Pro Ala Pro Pro Gln Val Leu Pro Gln Ala Pro Ala Pro Ala
625                 630                 635                 640

CCT GCT CCA GCC ATG GTA TCA GCT CTG GCC CAG GCC CCA GCC CCT GTC    1968
Pro Ala Pro Ala Met Val Ser Ala Leu Ala Gln Ala Pro Ala Pro Val
                645                 650                 655

CCA GTC CTA GCC CCA GGC CCT CCT CAG GCT GTG GCC CCA CCT GCC CCC    2016
Pro Val Leu Ala Pro Gly Pro Pro Gln Ala Val Ala Pro Pro Ala Pro
            660                 665                 670

AAG CCC ACC CAG GCT GGG GAA GGA ACG CTG TCA GAG GCC CTG CTG CAG    2064
```

```
Lys Pro Thr Gln Ala Gly Glu Gly Thr Leu Ser Glu Ala Leu Leu Gln
        675                 680                 685

CTG CAG TTT GAT GAT GAA GAC CTG GGG GCC TTG CTT GGC AAC AGC ACA     2112
Leu Gln Phe Asp Asp Glu Asp Leu Gly Ala Leu Leu Gly Asn Ser Thr
    690                 695                 700

GAC CCA GCT GTG TTC ACA GAC CTG GCA TCC GTC GAC AAC TCC GAG TTT     2160
Asp Pro Ala Val Phe Thr Asp Leu Ala Ser Val Asp Asn Ser Glu Phe
705                 710                 715                 720

CAG CAG CTG CTG AAC CAG GGC ATA CCT GTG GCC CCC CAC ACA ACT GAG     2208
Gln Gln Leu Leu Asn Gln Gly Ile Pro Val Ala Pro His Thr Thr Glu
                725                 730                 735

CCC ATG CTG ATG GAG TAC CCT GAG GCT ATA ACT CGC CTA GTG ACA GGG     2256
Pro Met Leu Met Glu Tyr Pro Glu Ala Ile Thr Arg Leu Val Thr Gly
            740                 745                 750

GCC CAG AGG CCC CCC GAC CCA GCT CCT GCT CCA CTG GGG GCC CCG GGG     2304
Ala Gln Arg Pro Pro Asp Pro Ala Pro Ala Pro Leu Gly Ala Pro Gly
        755                 760                 765

CTC CCC AAT GGC CTC CTT TCA GGA GAT GAA GAC TTC TCC TCC ATT GCG     2352
Leu Pro Asn Gly Leu Leu Ser Gly Asp Glu Asp Phe Ser Ser Ile Ala
    770                 775                 780

GAC ATG GAC TTC TCA GCC CTG CTG AGT CAG ATC AGC TCC TAA             2394
Asp Met Asp Phe Ser Ala Leu Leu Ser Gln Ile Ser Ser
785                 790                 795
```

(2) INFORMATION FOR SEQ ID NO:143:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 797 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:143:

```
Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu
 1               5                  10                  15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly
            20                  25                  30
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
        35                  40                  45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
    50                  55                  60
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65                  70                  75                  80
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
```

```
                    85                  90                  95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
            100                 105                 110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
        115                 120                 125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
    130                 135                 140
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145                 150                 155                 160
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
                165                 170                 175
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
            180                 185                 190
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
        195                 200                 205
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
    210                 215                 220
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys Ser
225                 230                 235                 240
Gly Leu Arg Ser Arg Ala Met Asp Glu Leu Phe Pro Leu Ile Phe Pro
                245                 250                 255
Ala Glu Pro Ala Gln Ala Ser Gly Pro Tyr Val Glu Ile Ile Glu Gln
            260                 265                 270
Pro Lys Gln Arg Gly Met Arg Phe Arg Tyr Lys Cys Glu Gly Arg Ser
        275                 280                 285
Ala Gly Ser Ile Pro Gly Glu Arg Ser Thr Asp Thr Thr Lys Thr His
    290                 295                 300
Pro Thr Ile Lys Ile Asn Gly Tyr Thr Gly Pro Gly Thr Val Arg Ile
305                 310                 315                 320
Ser Leu Val Thr Lys Asp Pro Pro His Arg Pro His Pro His Glu Leu
                325                 330                 335
Val Gly Lys Asp Cys Arg Asp Gly Phe Tyr Glu Ala Glu Leu Cys Pro
            340                 345                 350
Asp Arg Cys Ile His Ser Phe Gln Asn Leu Gly Ile Gln Cys Val Lys
        355                 360                 365
Lys Arg Asp Leu Glu Gln Ala Ile Ser Gln Arg Ile Gln Thr Asn Asn
    370                 375                 380
Asn Pro Phe Gln Val Pro Ile Glu Glu Gln Arg Gly Asp Tyr Asp Leu
385                 390                 395                 400
Asn Ala Val Arg Leu Cys Phe Gln Val Thr Val Arg Asp Pro Ser Gly
                405                 410                 415
Arg Pro Leu Arg Leu Pro Pro Val Leu Pro His Pro Ile Phe Asp Asn
            420                 425                 430
Arg Ala Pro Asn Thr Ala Glu Leu Lys Ile Cys Arg Val Asn Arg Asn
        435                 440                 445
Ser Gly Ser Cys Leu Gly Gly Asp Glu Ile Phe Leu Leu Cys Asp Lys
    450                 455                 460
Val Gln Lys Glu Asp Ile Glu Val Tyr Phe Thr Gly Pro Gly Trp Glu
465                 470                 475                 480
Ala Arg Gly Ser Phe Ser Gln Ala Asp Val His Arg Gln Val Ala Ile
                485                 490                 495
Val Phe Arg Thr Pro Pro Tyr Ala Asp Pro Ser Leu Gln Ala Pro Val
            500                 505                 510
Arg Val Ser Met Gln Leu Arg Arg Pro Ser Asp Arg Glu Leu Ser Glu
        515                 520                 525
Pro Met Glu Phe Gln Tyr Leu Pro Asp Thr Asp Asp Arg His Arg Ile
```


BNSDOCID: <WO___9845704A2_I_>

```
    530                 535                 540
Glu Glu Lys Arg Lys Arg Thr Tyr Glu Thr Phe Lys Ser Ile Met Lys
545                 550                 555                 560
Lys Ser Pro Phe Ser Gly Pro Thr Asp Pro Arg Pro Pro Pro Arg Arg
                565                 570                 575
Ile Ala Val Pro Ser Arg Ser Ser Ala Ser Val Pro Lys Pro Ala Pro
            580                 585                 590
Gln Pro Tyr Pro Phe Thr Ser Ser Leu Ser Thr Ile Asn Tyr Asp Glu
        595                 600                 605
Phe Pro Thr Met Val Phe Pro Ser Gly Gln Ile Ser Gln Ala Ser Ala
    610                 615                 620
Leu Ala Pro Ala Pro Pro Gln Val Leu Pro Gln Ala Pro Ala Pro Ala
625                 630                 635                 640
Pro Ala Pro Ala Met Val Ser Ala Leu Ala Gln Ala Pro Ala Pro Val
                645                 650                 655
Pro Val Leu Ala Pro Gly Pro Pro Gln Ala Val Ala Pro Pro Ala Pro
            660                 665                 670
Lys Pro Thr Gln Ala Gly Glu Gly Thr Leu Ser Glu Ala Leu Leu Gln
        675                 680                 685
Leu Gln Phe Asp Asp Glu Asp Leu Gly Ala Leu Leu Gly Asn Ser Thr
    690                 695                 700
Asp Pro Ala Val Phe Thr Asp Leu Ala Ser Val Asp Asn Ser Glu Phe
705                 710                 715                 720
Gln Gln Leu Leu Asn Gln Gly Ile Pro Val Ala Pro His Thr Thr Glu
                725                 730                 735
Pro Met Leu Met Glu Tyr Pro Glu Ala Ile Thr Arg Leu Val Thr Gly
            740                 745                 750
Ala Gln Arg Pro Pro Asp Pro Ala Pro Ala Pro Leu Gly Ala Pro Gly
        755                 760                 765
Leu Pro Asn Gly Leu Leu Ser Gly Asp Glu Asp Phe Ser Ser Ile Ala
    770                 775                 780
Asp Met Asp Phe Ser Ala Leu Leu Ser Gln Ile Ser Ser
785                 790                 795
```

CLAIMS

1. A method for extracting quantitative information relating to an influence on a cellular response, the method comprising recording variation, caused by the influence on a mechanically intact living cell or mechanically intact living cells, in spatially distributed light emitted from a luminophore, the luminophore being present in the cell or cells and being capable of being redistributed in a manner which is related with the degree of the influence, and/or of being modulated by a component which is capable of being redistributed in a manner which is related to the degree of the influence, the association resulting in a modulation of the luminescence characteristics of the luminophore, and processing the recorded variation in the spatially distributed light to provide quantitative information correlating the spatial distribution to the degree of the influence on the cellular response.

2. A method according to claim 1, as used for extracting quantitative information relating to an influence on an intracellular pathway involving redistribution of at least one component associated with the pathway, or part thereof, the method comprising recording the result of the influence on mechanically intact living cell or cells, as manifested in spatially distributed light emitted from a luminophore which is present in the cell or cells and which is capable of being redistributed, by modulation of the pathway, in a manner which is related to the redistribution of the at least one component of the intracellular pathway, processing the recorded result to provide quantitative information about the spatially distributed light and correlating the quantitative information to the degree of the influence on the intracellular pathway.

3. A method according to claim 1 or 2, wherein the quantitative information which is indicative of the degree of the cellular response to the influence or the result of the influence on the intracellular pathway is extracted from the recording or recordings according to a predetermined calibration based on responses or results, recorded in the same manner, to known degrees of a relevant specific influence.

4. A method according to any of the preceding claims, wherein the influence is contact between the mechanically intact living cell or the group of mechanically intact living cells with a

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chemical substance and/or incubation of the mechanically intact living cell or the group of mechanically intact living cells with a chemical substance.

5. A method according to claim 4 wherein the substance is a substance whose effect on an intracellular pathway is to be determined.

6. A method according to any of the preceding claims, wherein the recording is made at a single point in time after the application of the influence.

7. A method according to any of claims 1-5, wherein the recording is made at two points in time, one point being before, and the other point being after the application of the influence.

8. A method according to any of claims 1-5, wherein the recording is performed at a series of points in time, in which the application of the influence occurs at some time after the first time point in the series of recordings, the recording being performed, e.g., with a predetermined time spacing of from 0.1 seconds to 1 hour, preferably from 1 to 60 seconds, more preferably from 1 to 30 seconds, in particular from 1 to 10 seconds, over a time span of from 1 second to 12 hours, such as from 10 seconds to 12 hours, e.g., from 10 seconds to one hour, such as from 60 seconds to 30 minutes or 20 minutes.

9. A method according to any of claims 1-7, wherein the cell or cells is/are fixed at a point in time after the application of the influence at which the response has been predetermined to be significant, and the recording is made at an arbitrary later time.

10. A method according to any of the preceding claims, wherein the luminophore is a luminophore which is capable of being redistributed in a manner which is physiologically relevant to the degree of the influence.

11. A method according to any of the preceding claims, wherein the luminophore is a luminophore which is capable of associating with a component which is capable of being redistributed in manner which is physiologically relevant to the degree of the influence.

12. A method according to any of the preceding claims, wherein the luminophore is a luminophore which is capable of being redistributed in a manner which is experimentally determined to be correlated to the degree of the influence.

13. A method according to any of the preceding claims, wherein the luminophore is a luminophore which is capable of being redistributed, by modulation of the intracellular pathway, in substantially the same manner as the at least one component of the intracellular pathway.

14. A method according to any of claims 1-13, wherein the luminophore is a luminophore which is capable of being quenched upon spatial association with a component which is redistributed by modulation of the pathway, the quenching being measured as a decrease in the intensity of the luminescence.

15. A method according to any of claims 1-13, wherein the variation or result with respect to the spatially distributed light emitted by the luminophore is detected by a change in the resonance energy transfer between the luminophore and another luminescent entity capable of delivering energy to the luminophore, each of which has been selected or engineered to become part of, bound to or associated with particular components of the intracellular pathway, and one of which undergoes redistribution in response to the influence, thereby changing the amount of resonance energy transfer, the change in the resonance energy transfer being measured as a change in the intensity of emission from the luminophore.

16. A method according to claim 15, wherein the change in the intensity of the emission from the luminophore is sensed by a single channel photodetector which responds only to the average intensity of the luminophore in a non-spatially resolved fashion

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17. A method according to any of claims 1-16, wherein the property of the light being recorded is intensity, fluorescence lifetime, polarization, wavelength shift, or other property which is modulated as a result of the underlying cellular response.

18. A method according to any of claims 1-15 or 17, wherein the recording of the spatially distributed light is performed using a recording system which records the spatial distribution of a recordable property of the light in the form of an ordered array of values.

19. A method according to claim 18, wherein the recording of the spatial distribution of the recordable property of the light is performed using a charge transfer device such as a CCD array or a vacuum tube device such as a vidicon tube.

20. A method according to any of the preceding claims, wherein the light to be measured passes through a filter which selects the desired component of the light to be measured and rejects other components.

21. A method according to any of the preceding claims, wherein the recording of the spatial distribution of the recordable property of light is performed by fluorescence microscopy.

22. A method according to any of the preceding claims, wherein the recording of the variation or result with respect to light emitted from the luminophore is performed by recording the spatially distributed light as one or more digital images, and the processing of the recorded variation to reduce it to one or more numbers representative of the degree of redistribution comprises a digital image processing procedure or combination of digital image processing procedures.

23. A method according to any of claims 2-22, wherein the intracellular pathway is an intracellular signalling pathway.

24. A method according to any of the preceding claims, wherein the luminophore is a fluorophore.

25. A method according to any of the preceding claims wherein the luminophore is a polypeptide encoded by and expressed from a nucleotide sequence harboured in the cell or cells.

26. A method according to any of the preceding claims, wherein the luminophore is a hybrid polypeptide comprising a fusion of at least a portion of each of two polypeptides one of which comprises a luminescent polypeptide and the other one of which comprises a biologically active polypeptide, as defined herein.

27. A method according to claim 26, wherein the luminescent polypeptide is a GFP as defined herein.

28. A method according to claim 27 wherein the GFP is selected from the group consisting of green fluorescent proteins having the F64L mutation as defined herein.

29. A method according to claim 28 wherein the GFP is a GFP variant selected from the group consisting of F64L-GFP, F64L-Y66H-GFP, F64L-S65T-GFP, and EGFP.

30. A method according to any of the previous claims for detecting intracellular translocation of a biologically active polypeptide affecting intracellular processes upon activation, the method comprising

a) culturing one or more cells containing a nucleotide sequence coding for a hybrid polypeptide comprising a GFP which is N- or C-terminally tagged, optionally through a linker, to a biologically active polypeptide under conditions permitting expression of the nucleotide sequence,

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b) modulating the activity of the biologically active polypeptide by incubating the cell or cells with a substance having biological activity and

c) measuring the fluorescence produced by the incubated cell or cells and determining the result or variation with respect to the fluorescence, such result or variation being indicative of the translocation of a biologically active polypeptide in said cell.

31. A method according to claim 30, wherein the nucleotide sequence is a DNA sequence.

32. A method according to claim 30 or 31, wherein the modulation is an activation.

33. A method according to claim 30 or 31, wherein the modulation is a deactivation.

34. A method according to any of claims 30-33 wherein the fluorescence of the cell or cells is measured prior to the modulation, and the result or variation determined in step (c) is a change in fluorescence compared to the fluorescence measured prior to the modulation.

35. A method according to any of claims 30-34, wherein the intracellular processes are intracellular signalling pathways.

36. A method according to claim 34, wherein the change in fluorescence measured in step (c) comprises determining a change in the spatial distribution of the fluorescence.

37. A method according to any of the preceding claims wherein the mechanically intact living cell or cells is/are a mammalian cell/mammalian cells which, during the time peroid over which the influence is observed, is/are incubated at a temperature of 30°C or above, preferably at a temperature of from 32°C to 39°C, more preferably at a temperature of from 35°C to 38°C, and most preferably at a temperature of about 37°C.

38. A method according to any of the preceding claims, wherein the at least one mechanically intact living cell is part of a matrix of identical or non-identical cells.

39. A method according to any of claims 1-36 and 38, wherein the cell or cells is/are selected from the group consisting of fungal cells, such as a yeast cell; invertebrate cells including insect cells; and vertebrate cells, such as mammalian cells.

40. A nucleic acid construct coding for a fusion polypeptide comprising a biologically active polypeptide that is a component of an intracellular signalling pathway, or a part thereof, and a GFP, with the proviso that the construct is not a construct coding for a fusion polypeptide in which the biologically active polypeptide is selected from the group consisting of PKC-alpha, PKC-gamma, and PKC-epsilon.

41. A nucleic acid construct coding for a fusion polypeptide comprising a biologically active polypeptide that is a component of an intracellular signalling pathway, or a part thereof, and an F64L mutant of GFP.

42. A nucleic acid construct according to claim 40 or 41, wherein the biologically active polypeptide is a protein kinase or a phosphatase.

43. A nucleic acid construct according to any of claims 40-42 wherein the GFP is N- or C-terminally tagged, optionally via a peptide linker, to the biologically active polypeptide or part thereof.

44. A nucleic acid construct according to any of claims 40, 41 and 43, wherein the biologically active polypeptide is a transcription factor or a part thereof which changes cellular localisation upon activation.

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45. A nucleic acid construct according to any of claims 40, 41 and 43, wherein the biologically active polypeptide is a protein, or a part thereof, which is associated with the cytoskeletal network and which changes cellular localisation upon activation.

46. A nucleic acid construct according to any of claims 40-43, wherein the biologically active polypeptide is a protein kinase or a part thereof which changes cellular localisation upon activation.

47. A nucleic acid construct according to claim 46, wherein the protein kinase is a serine/threonine protein kinase or a part thereof capable of changing intracellular localisation upon activation.

48. A nucleic acid construct according to claim 46, wherein the protein kinase is a tyrosine protein kinase or a part thereof capable of changing intracellular localisation upon activation.

49. A nucleic acid construct according to claim 46, wherein the protein kinase is a phospholipid-dependent serine/threonine protein kinase or a part thereof capable of changing intracellular localisation upon activation.

50. A nucleic acid construct according to claim 46, wherein the protein kinase is a cAMP-dependent protein kinase or a part thereof capable of changing cellular localisation upon activation.

51. A nucleic acid construct according to claim 50 which codes for a PKAc-F64L-S65T-GFP fusion.

52. A nucleic acid construct according to claim 46, wherein the protein kinase is a cGMP-dependent protein kinase or a part thereof capable of changing cellular localisation upon activation.

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53. A nucleic acid construct according to claim 46, wherein the protein kinase is a calmodulin-dependent serine/threonine protein kinase or a part thereof capable of changing cellular localisation upon activation.

54. A nucleic acid construct according to claim 46, wherein the protein kinase is a mitogen-activated serine/threonine protein kinase or a part thereof capable of changing cellular localisation upon activation.

55. A nucleic acid construct according to claim 54, which codes for an ERK1-F64L-S65T-GFP fusion.

56. A nucleic acid construct according to claim 54, which codes for an EGFP-ERK1 fusion.

57. A nucleic acid construct according to claim 46, wherein the protein kinase is a cyclin-dependent serine/threonine protein kinase or a part thereof capable of changing cellular localisation upon activation.

58. A nucleic acid construct according to claim 42 or 43, wherein the biologically active polypeptide is a protein phosphatase or a part thereof capable of changing cellular localisation upon activation.

59. A nucleic acid construct according to any of claims 40-58 which is a DNA construct.

60. A nucleic acid construct according to any of claims 40-59 wherein the gene encoding GFP is derived from Aequorea victoria.

61. A nucleic acid construct according to claim 60 in which the gene encoding GFP is the gene encoding EGFP as defined herein.

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62. A nucleic acid construct according to claim 60 in which the gene encoding a GFP is a gene encoding a GFP variant selected from F64L-GFP, F64L-Y66H-GFP and F64L-S65T-GFP.

63. A DNA construct according to claim 59 and 61 or, where applicable, 62, which is a construct as identified by any of the DNA sequences shown in SEQ ID NO: 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, and 142, or is a variant thereof capable of encoding the same fusion polypeptide or a fusion polypeptide which is biologically equivalent thereto, as defined herein.

64. A cell containing a nucleic acid construct according to any of claims 40-63 and capable of expressing the sequence encoded by the construct.

65. A cell according to claim 64, which is a eukaryotic cell.

66. A cell according to claim 64, which is selected from the group consisting of fungal cells, such as yeast cells; invertebrate cells, including insect cells, and vertebrate cells, such as mammalian cells.

67. A cell according to claim 66, which is a mammalian cell.

68. An organism carrying in at least one of its component cells a nucleic acid sequence as contained in the constructs according to any of claims 40-59, said cell being capable of expressing said nucleic acid sequence.

69. An organism according to claim 68 which is selected from the group consisting of unicellular and multicellular organisms, such as a mammal.

70. A fluorescent probe comprising a GFP which is N- or C-terminally tagged, optionally via a peptide linker, to a biologically active polypeptide or a part or a subunit thereof which is a component of a intracellular signalling pathway as defined herein, the probe being a probe which is encoded by the nucleic acid construct according to any of claims 40-59.

71. A method according to any of claims 1-39, wherein the luminophore is a fusion polypeptide as encoded by the nucleic acid construct according to any of claims 40-63.

72. A method according to any of claims 1-39 or 71 in which the method of the invention is used in a screening program as defined herein.

73. An apparatus for measuring the distribution of fluorescence in at least one cell, and thereby any change in the distribution of fluorescence in at least one cell, which includes the following component parts: (a) a light source, (b) a means for selecting the wavelength(s) of light from the source which will excite the fluorescence of the protein, (c) a means for rapidly blocking or pass ing the excitation light into the rest of the system, (d) a series of optical elements for conveying the excitation light to the specimen, collecting the emitted fluorescence in a spatially resolved fashion, and forming an image from this fluorescence, (e) a bench or stand which holds the container of the cells being measured in a predetermined geometry with respect to the series of optical elements, (f) a detector to record the spatially resolved fluorescence in the form of an image, (g) a computer or electronic system and associated software to acquire and store the recorded images, and to compute the degree of redistribution from the recorded images.

74. An apparatus according to claim 73 in which some or all of the system is automated.

75. An apparatus according to claim 73 in which components d and e comprise a fluorescence microscope.

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76. An apparatus according to claim 73 in which component f is a CCD camera.

77. An apparatus according to claim 73 in which the image is formed and recorded by an optical scanning system.

78. An apparatus according to claim 73 in which a liquid addition system is used to add a known or unknown compound to any or all of the cells in the cell holder at a time determined in advance.

79. An apparatus according to claim 78 in which the liquid addition system is under the control of the computer or electronic system.

80. A method according to any of claims 1-79 wherein the method is a screening program for the identification of a biologically active substance as defined herein that directly or indirectly affects an intracellular signalling pathway and is potentially useful as a medicament, wherein the result of the individual measurement of each substance being screened which indicates its potential biological activity is based on measurement of the redistribution of spatially resolved luminescence in living cells and which undergoes a change in distribution upon activation of an intracellular signalling pathway.

81 A method according to any of claims 1-79 wherein the method is a screening program for the identification of a biologically toxic substance as defined herein that exerts its toxic effect by interfering with an intracellular signalling pathway, wherein the result of the individual measurement of each substance being screened which indicates its potential biologically toxic activity is based on measurement of the redistribution of said fluorescent probe in living cells and which undergoes a change in distribution upon activation of an intracellular signalling pathway.

82. A method according to any of claims 1-80 wherein a fluorescent probe is used in backtracking of signal transduction pathways as defined herein.

83. A method of treating a condition or disease related to the intracellular function of a protein kinase comprising administering to a patient suffering from said condition or disease an effective amount of a compound which has been discovered by any method according to the invention.

84. A compound that modulates a component of an intracellular pathway as defined herein, as determined by a method according to the method of the invention.

85. A medical composition comprising a therapeutic amount of a compound identified according the method of the invention.

86. A method of selectively treating a patient suffering from an ailment which responds to medical treatment comprising obtaining a primary cell or cells from said patient, transfecting the cell or cells with at least one DNA sequence encoding a fluorescent probe according to the invention, culturing the cell or cells under conditions permitting the expression of said probes and exposing it to an array of medicaments suspected of being capable of alleviating said ailment, then comparing changes in fluorescence patterns or redistribution patterns of the fluorescent probes in the intact living cell or cells to detect the cellular response to the specific medicaments (obtaining a cellular action profile), then selecting a medicament(s) based on desired activity and acceptable level of side effects and administering an effective amount of said medicament(s) to said patient.

87. A method according to any of claims 1-80 of identifying a drug target among the group of biologically active polypeptides which are components of intracellular signalling pathways.

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Fig 1

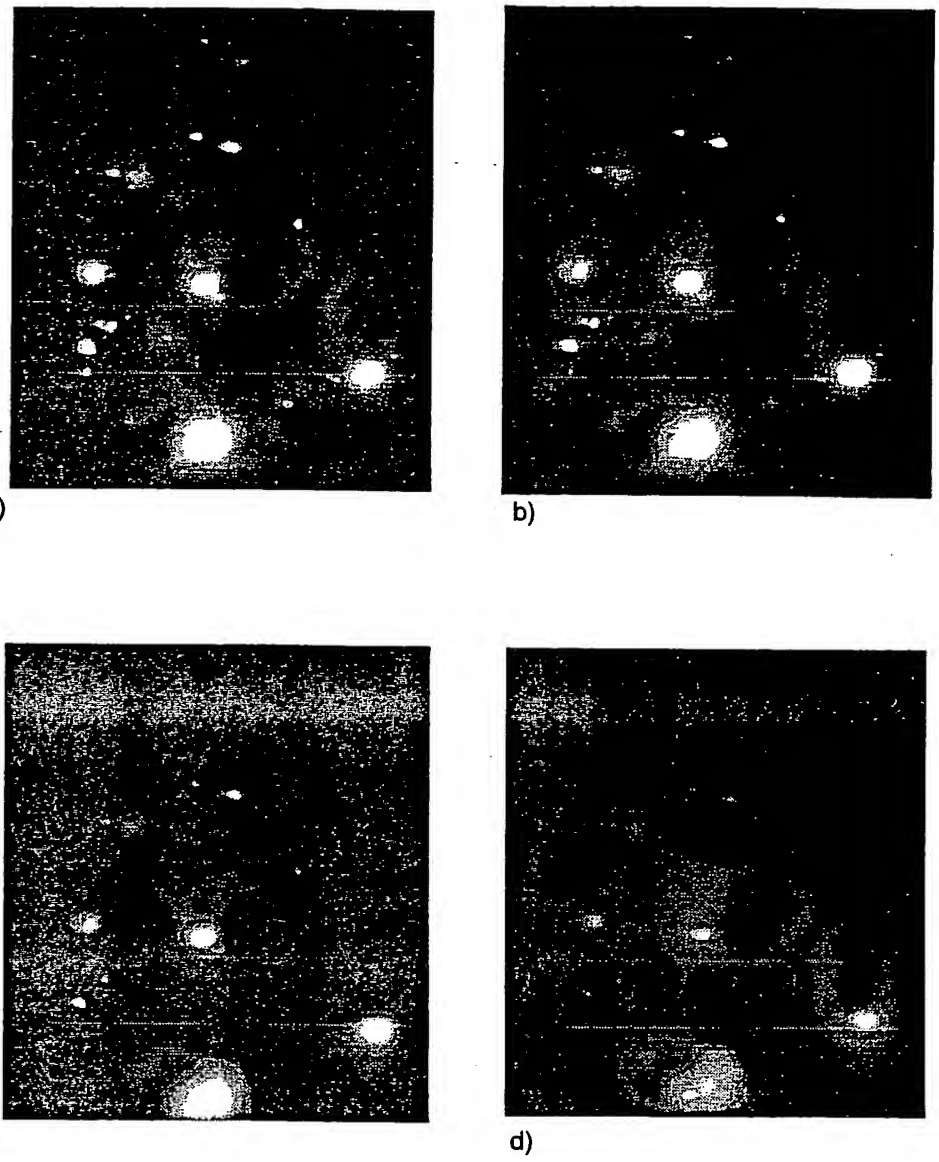

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Fig 2

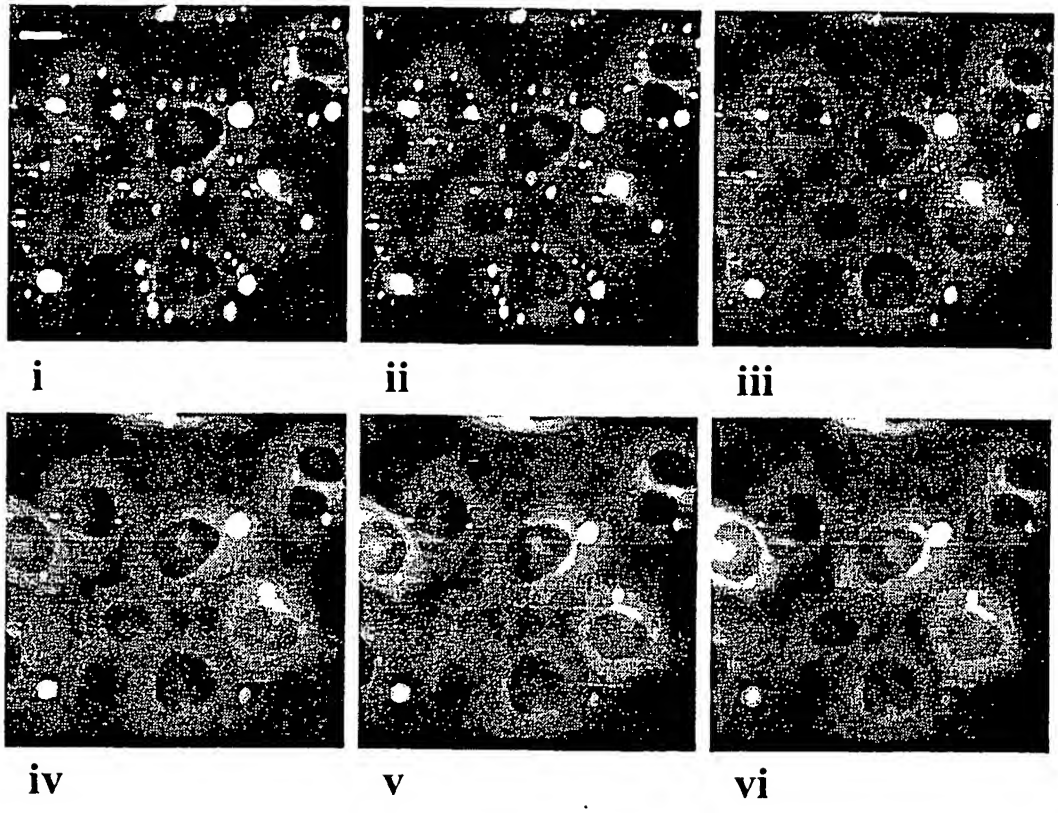

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Fig 3

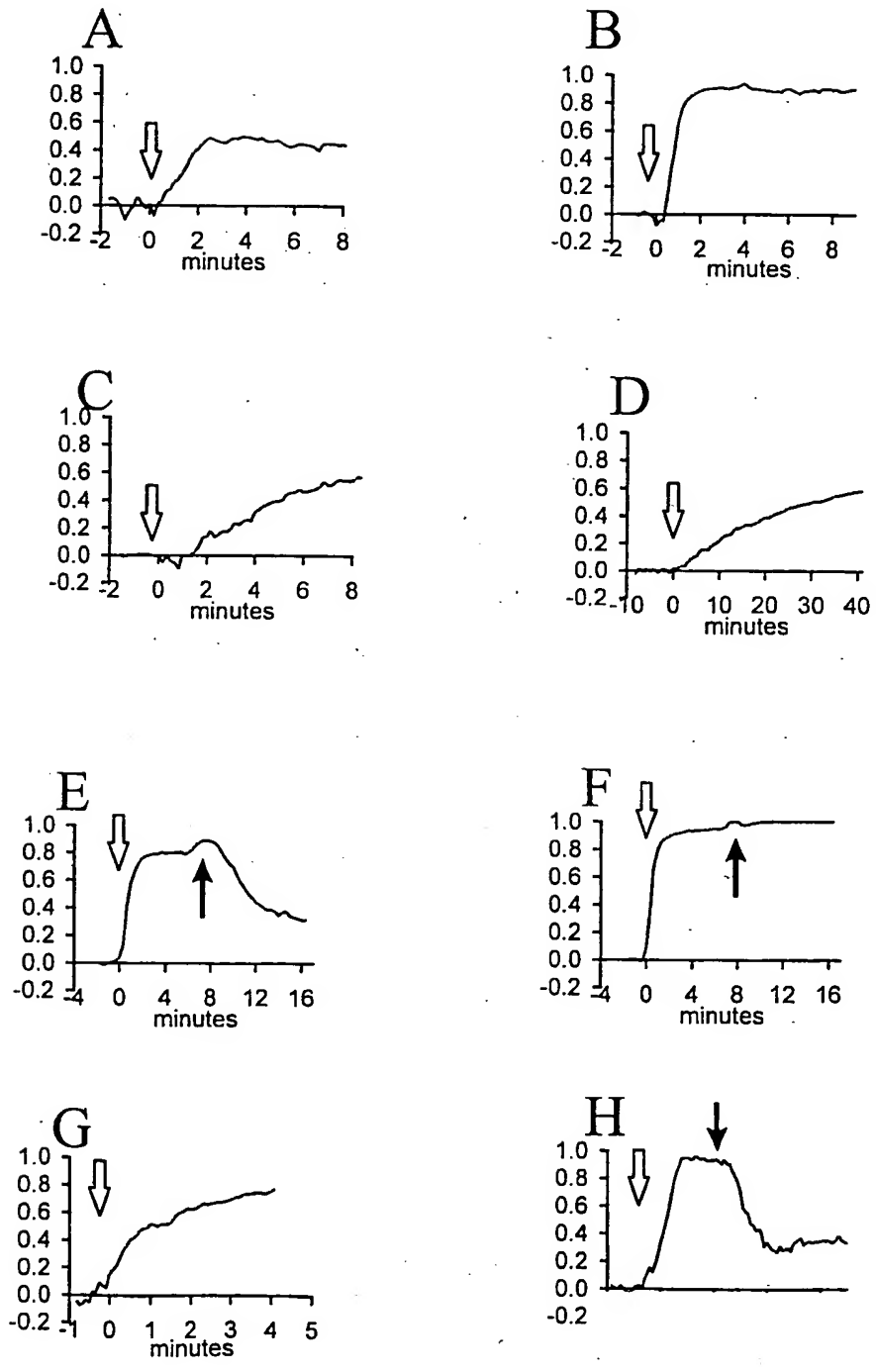

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Fig 4

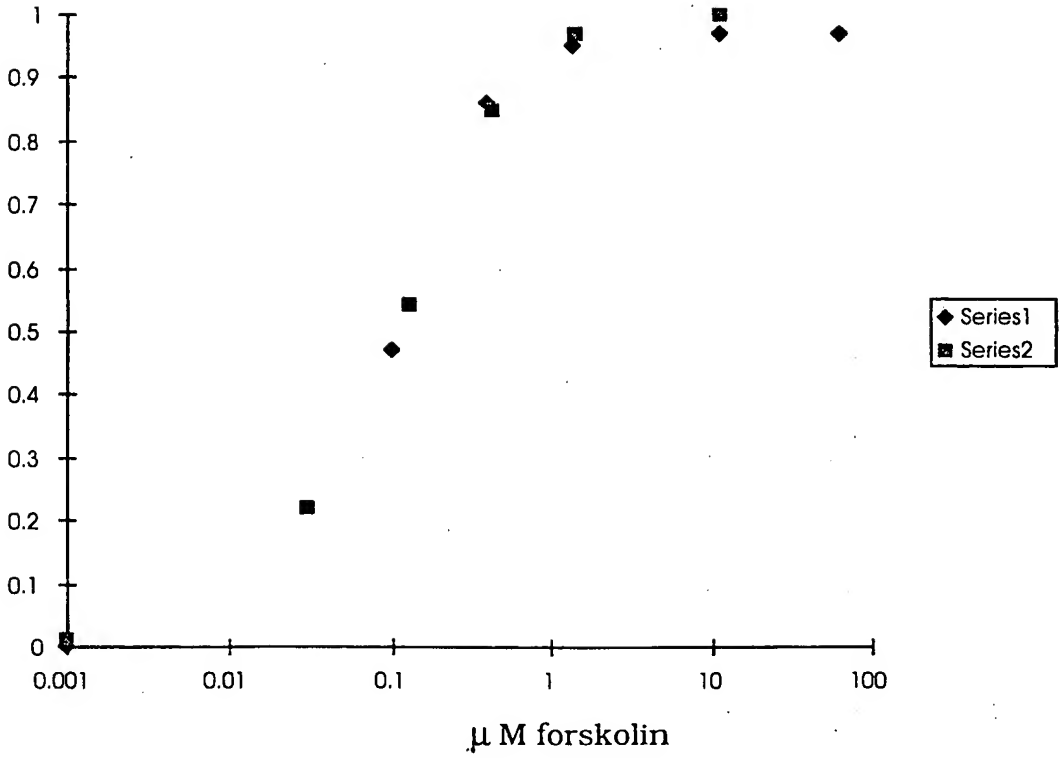

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Fig 5

[forskolin]µM	$t_{1/2max}$ / s	t_{max} / s
1	115±21	310±31
10	69±14	224±47
50	47±10	125±28

Fig 6

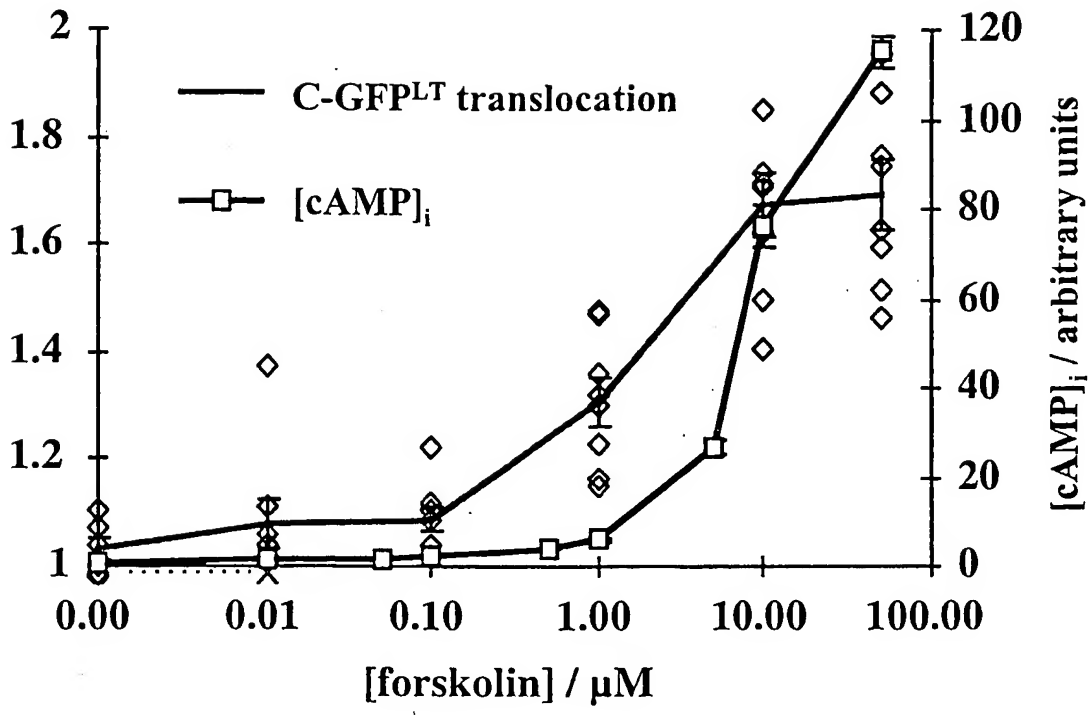

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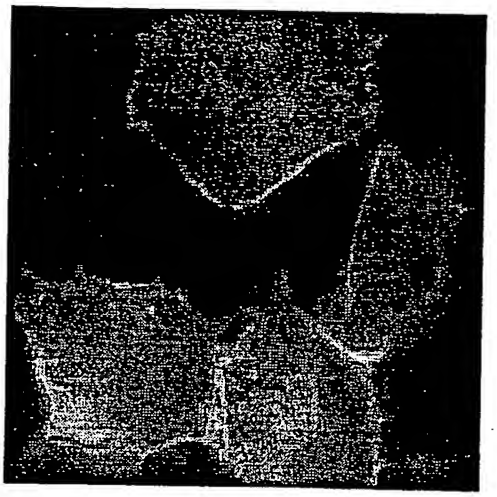
Fig 7

a)



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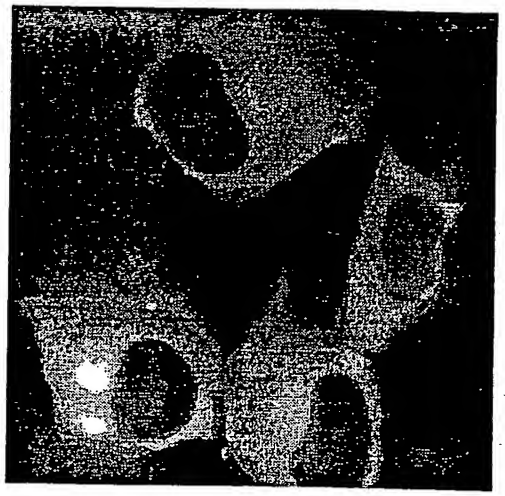

c)

Fig 8

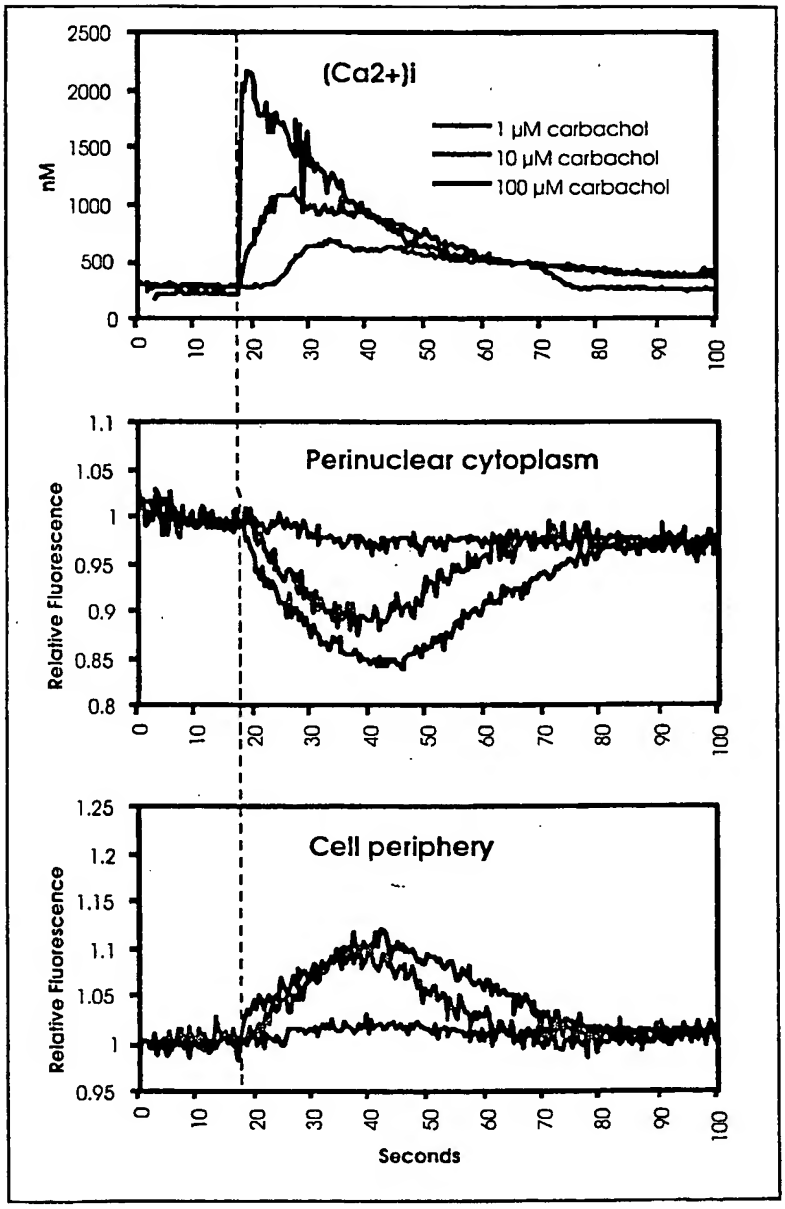

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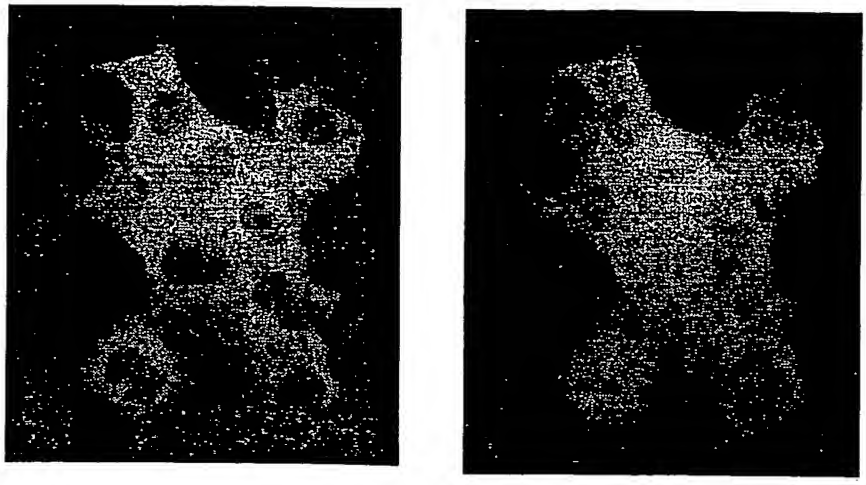
Fig 9



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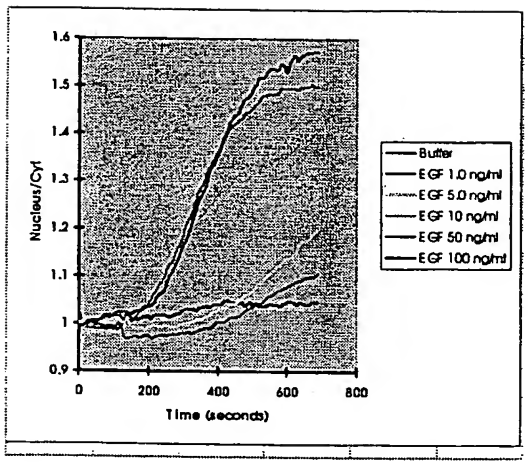

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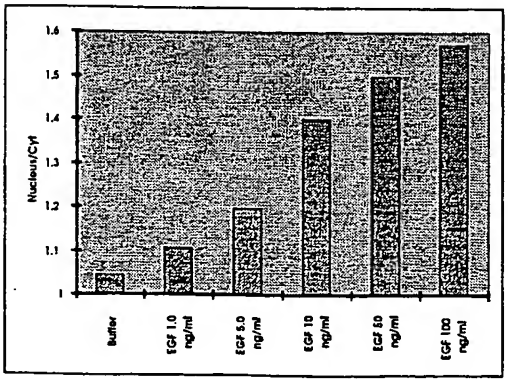

d)

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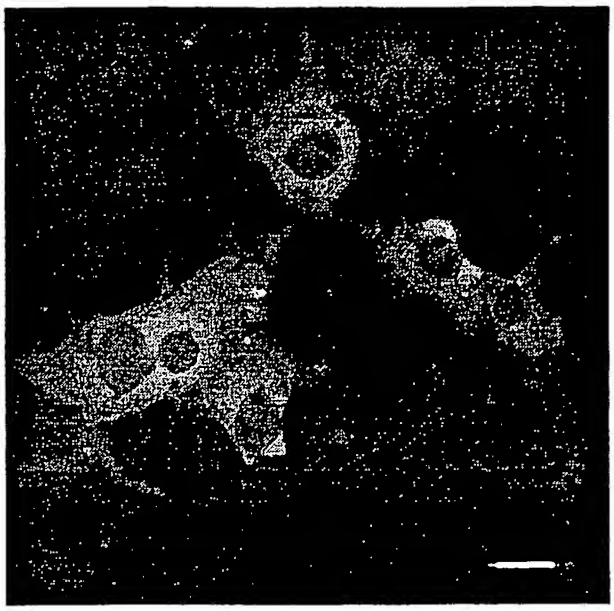
Fig 10

a)



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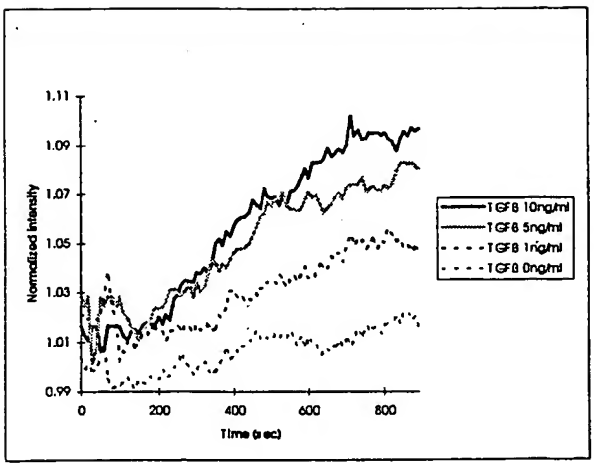

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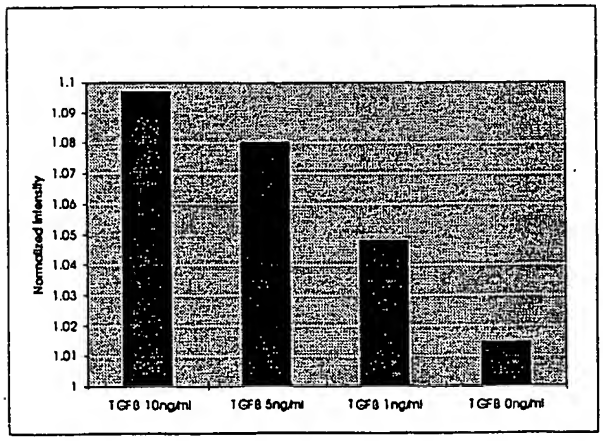

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Fig 11

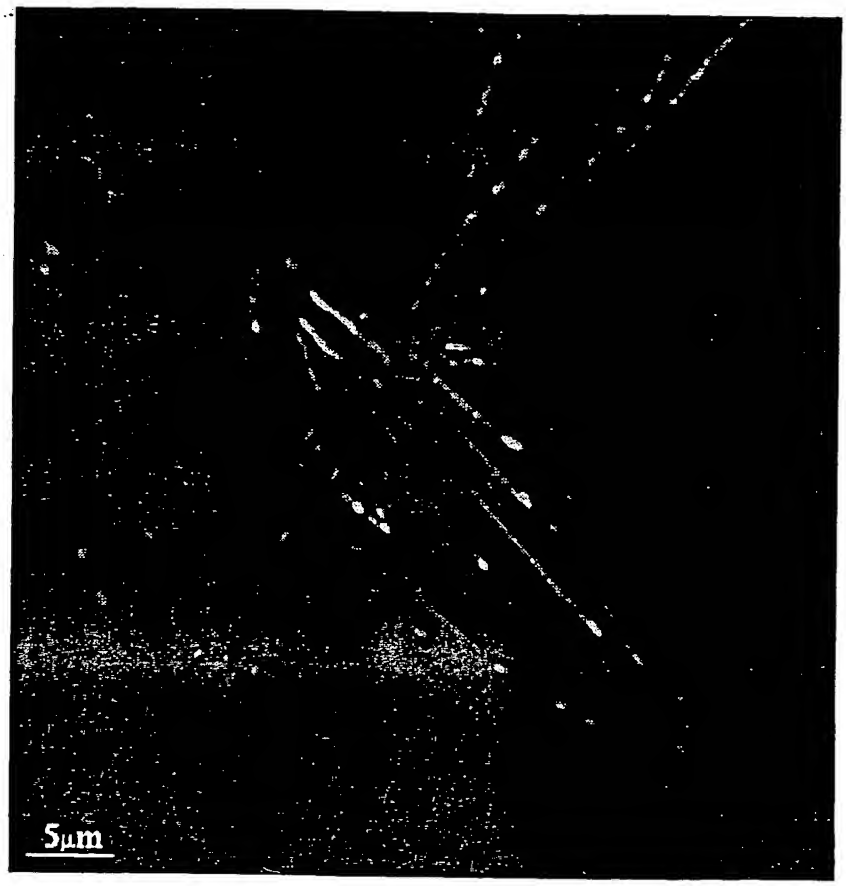

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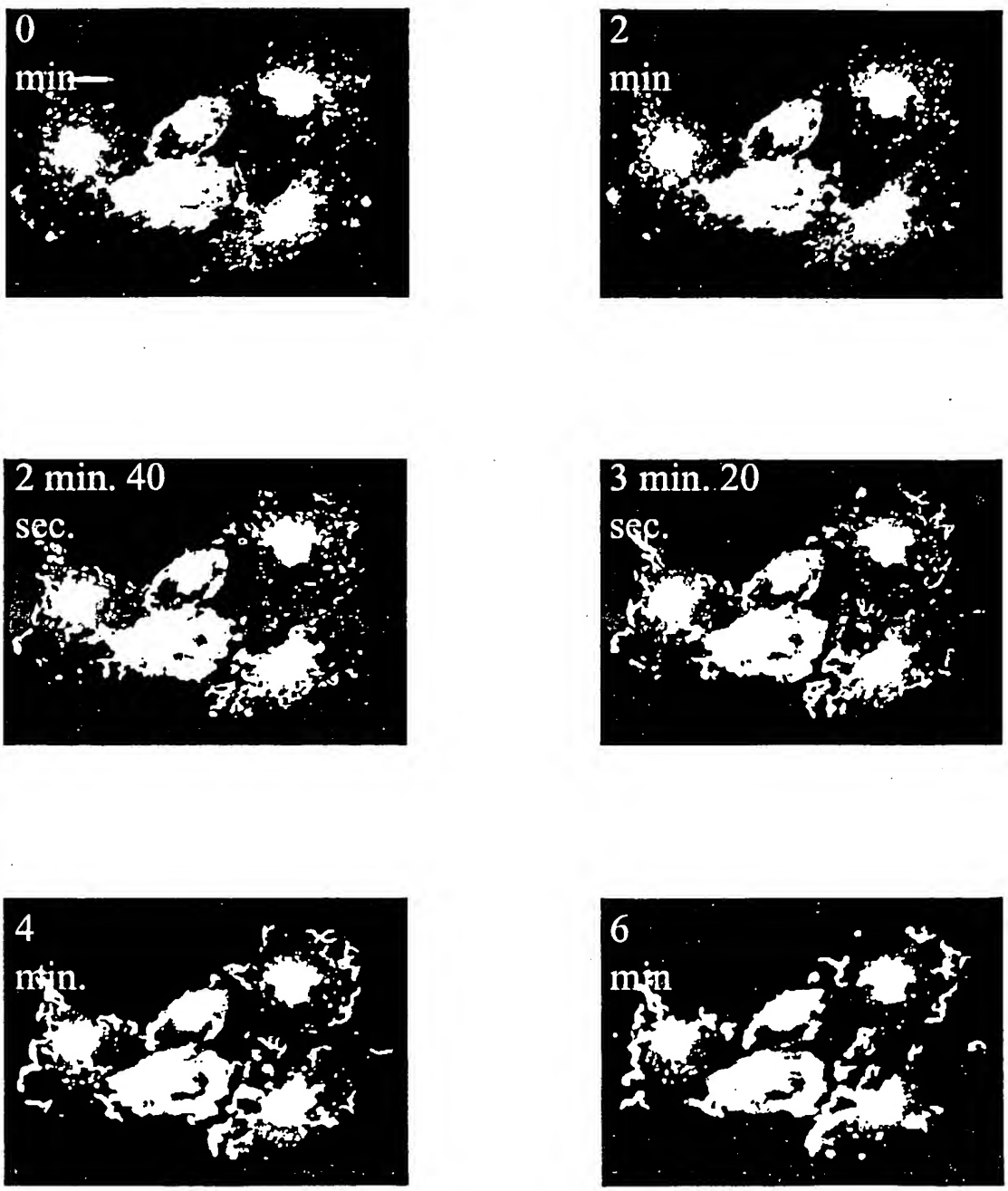
Fig. 12



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(54) Title: A METHOD FOR EXTRACTING QUANTITATIVE INFORMATION RELATING TO AN INFLUENCE ON A CELLULAR RESPONSE

(57) **Abstract**

Cells are genetically modified to expresss a luminophore, e.g., a modified (F64L, S65T, Y66H) Green Fluorescent Protein (GFP, EGFP) coupled to a component of an intracellular signalling pathway such as a transcription factor, a cGMP- or cAMP-dependent protein kinase, a cyclin-, calmodulin- or phospholipid-dependent or mitogen-activated serine/threonin protein kinase, a tyrosine protein kinase, or a protein phosphatase (e.g. PKA, PKC, Erk, Smad, VASP, actin, p38, Jnk1, PKG, IkappaB, CDK2, Grk5, Zap70, p85, protein-tyrosine phosphatase 1C, Stat5, NFAT, NFkappaB, RhoA, PKB). An influence modulates the intracellular signalling pathway in such a way that the luminophore is being redistributed or translocated with the component in living cells in a manner experimentally determined to be correlated to the degree of the influence. Measurement of redistribution is performed by recording of light intensity, fluorescence lifetime, polarization, wavelength shift, resonance energy transfer, or other properties by an apparatus consisting of e.g. a fluorescence microscope and a CCD camera. Data stored as digital images are processed to numbers representing the degree of redistribution. The method can be used as a screening program for identifying a compound that modulates a component and is capable of treating a disease related to the function of the component.

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INTERNATIONAL SEARCH REPORT

Int. tional Application No
PCT/DK 98/00145

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 G01N33/50 C12Q1/48 C12Q1/25

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 G01N C12Q C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 11094 A (NOVONORDISK AS ;THASTRUP OLE (DK); TULLIN SOEREN (DK); POULSEN LAR) 27 March 1997 see the whole document	1-27, 30-40, 44-60, 64-82,88
Y	see claims	28,29, 41,61-63

X	WO 91 01305 A (UNIV WALES MEDICINE) 7 February 1991 see page 4, line 15 - line 20	1-27, 30-40, 42-60, 64-84, 87,88
Y	see claims see examples 1-10	28,29, 41,61-63
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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
19 January 1999	25. 02. 1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Hoekstra, S

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Int ational Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category '	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95 07463 A (UNIV COLUMBIA ;WOODS HOLE OCEANOGRAPHIC INST (US); CHALFIE MARTIN) 16 March 1995 cited in the application see claim 26	1-27, 30-40, 42-60, 64-84, 87,88
Y	see the whole document	28,29, 41,61-63

Y	WO 96 23898 A (NOVONORDISK AS ;THASTRUP OLE (DK); TULLIN SOEREN (DK); POULSEN LAR) 8 August 1996 see the whole document	28,29, 41,61-63
X	see page 8-17	42,43, 46,47

X	WO 96 03649 A (UNIV NORTH CAROLINA) 8 February 1996 see page 49; example 6.10	45

P,X	WO 97 20931 A (US HEALTH ;HTUN HAN (US); HAGER GORDON L (US)) 12 June 1997 see claims 41-58	40,44

P,X	WO 97 30074 A (CYTOGEN CORP ;UNIV NORTH CAROLINA (US)) 21 August 1997 see page 57	44

P,X	WO 98 02571 A (TSIEN ROGER Y ;CUBITT ANDREW B (US); UNIV CALIFORNIA (US)) 22 January 1998 see claims	1-27, 30-40, 42-50, 52-54, 57-60, 64-82,88

E	WO 98 30715 A (ISACOFF EHUD Y ;SIEGAL MICAH S (US); UNIV CALIFORNIA (US); CALIFOR) 16 July 1998 see the whole document	1-84,87, 88

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INTERNATIONAL SEARCH REPORT

Int ational Application No
PCT/DK 98/00145

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
P,X	SAKAI, N. ET AL.: "Direct visualization of the translocation of the gamma subspecies of protein kinase c in living cells using fusion proteins with green fluorescent protein." THE JOURNAL OF CELL BIOLOGY, vol. 139, no. 6, 15 December 1997, pages 1465-1476, XP002078902 see the whole document	1-43,46, 47,49, 53-57, 59-82,88
O,X	& Direct visualization of the translocation of the gamma subspecies of protein kinase c in living cells using fusion proteins with green fluorescent protein.Meeting held at 22-23.03.97 cited in the application see abstract	

X	SCHMIDT, D.J. ET AL.: "Dynamic analysis of alpha-PKC-GFP chimera translocation events in smooth muscle with ultra-high speed 3D fluorescence microscopy" FASEB JOURNAL, vol. 11, no. 3, 28 February 1997, page A505 XP002077257 cited in the application see abstract	1-43,46, 47,49, 53-57, 59-82,88

X	GERISCH, GUENTHER ET AL: "Chemoattractant-controlled accumulation of coronin at the leading edge of Dictyostelium cells monitored using a green fluorescent protein-coronin fusion protein" CURR. BIOL. (1995), 5(11), 1280-5 CODEN: CUBLE2;ISSN: 0960-9822, XP002089510 see abstract p 1281, right col, second full , last sentence	1,40,43, 45

X	SIDOROVA, JULIA M. ET AL: "Cell cycle-regulated phosphorylation of Swi6 controls its nuclear localization" MOL. BIOL. CELL (1995), 6(12), 1641-58 CODEN: MBCEEV;ISSN: 1059-1524, XP002089512 see the whole document	40,43,44

X	HAN HTUN ET AL: "VISUALIZATION OF GLUCOCORTICOID RECEPTOR TRANSLOCATION AND INTRANUCLEAR ORGANIZATION IN LIVING CELLS WITH A GREEN FLUORESCENT PROTEIN CHIMERA" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 93, no. 10, May 1996, pages 4845-4850, XP002029560 see the whole document	1-40,44, 64-72

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INTERNATIONAL SEARCH REPORT

In. .ational Application No
PCT/DK 98/00145

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication where appropriate, of the relevant passages	Relevant to claim No.
X	CAREY K L ET AL: "EVIDENCE USING A GREEN FLUORESCENT PROTEIN-GLUCOCORTICOID RECEPTOR CHIMERA THAT THE RAN/TC4 GTPASE MEDIATES AN ESSENTIAL FUNCTION INDEPENDENT OF NUCLEAR PROTEIN IMPORT" THE JOURNAL OF CELL BIOLOGY, vol. 133, no. 5, June 1996, pages 985-996, XP000670316 cited in the application see the whole document	1-40,44, 64-72
X	OGAWA H ET AL: "LOCALIZATION, TRAFFICKING, AND TEMPERATURE-DEPENDENCE OF THE AEQUOREA GREEN FLUORESCENT PROTEIN IN CULTURES VERTEBRATE CELLS" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 92, no. 25, 5 December 1995, pages 11899-11903, XP002029556 see the whole document	1-40,44, 64-72
X	WESTPHAL, MONIKA ET AL: "Microfilament dynamics during cell movement and chemotaxis monitored using a GFP - actin fusion protein" CURR. BIOL. (1997), 7(3), 176-183 CODEN: CUBLE2;ISSN: 0960-9822, XP002090291 see page 181, left-hand column, line 1	1,40,43, 45
X	TODA, TAKASHI ET AL: "The fission yeast sts5+ gene is required for maintenance of growth polarity and functionally interacts with protein kinase C and an osmosensing MAP kinase pathway" J. CELL SCI. (1996), 109(9), 2331-2342 CODEN: JNCSAI;ISSN: 0021-9533, XP002090292 see abstract	40,42
A	WEBB, CHRIS D. ET AL: "Use of green fluorescent protein for visualization of cell-specific gene expression and subcellular protein localization during sporulation in Bacillus subtilis" J. BACTERIOL. (1995), 177(20), 5906-11 CODEN: JOBAAY;ISSN: 0021-9193, XP002089513 see the whole document	44
A	WO 94 23039 A (CANCER RES INST ROYAL ;MARSHALL CHRISTOPHER JOHN (GB); ASHWORTH AL) 13 October 1994 see the whole document	1-84,87, 88

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INTERNATIONAL SEARCH REPORT

Ir. ational application No.
PCT/DK 98/00145

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 83-84 and claim 87 relate to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition (Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy).

2. [X] Claims Nos.: 85,86
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [X] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[X] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Claims Nos.: 85,86

The subject-matter (compounds per se) is solely characterised in claims 85 and 86 by the result to be achieved, no support of a technical character is derivable from the description for the technical formulation of the subject of the search, accordingly no scope of a search could be defined and a meaningfull search is hence not possible.

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: Partially: 1-43, 46, 59-82 and 88; Entirely: 47, 49, 53-57

Methods for extracting information from influences on a living cell involving observing spatial redistribution or modulation of a luminophore linked to a biologically active molecule, in particular to a molecule involved in intracellular signalling pathways, nucleic acids encoding fusion proteins comprising bothe the luminophore and the biological active molecule, cells containing and expressing these nucleic acids, as well as methods and apparatuses involving above products, inso far as related to the biologically active protein being serine/threonine protein kinases

2. Claims: Partially: 1-41, 43, 59-82 and 88; Entirely: 48

Methods for extracting information from influences on a living cell involving observing spatial redistribution or modulation of a luminophore linked to a biologically active molecule, in particular to a molecule involved in intracellular signalling pathways, nucleic acids encoding fusion proteins comprising bothe the luminophore and the biological active molecule, cells containing and expressing these nucleic acids, as well as methods and apparatuses involving above products, inso far as related to the biologically active protein being to tyrosine kinases

3. Claims: Partially: 1-43, 46, 59-82 and 88; Entirely: 50, 51

MMethods for extracting information from influences on a living cell involving observing spatial redistribution or modulation of a luminophore linked to a biologically active molecule, in particular to a molecule involved in intracellular signalling pathways, nucleic acids encoding fusion proteins comprising bothe the luminophore and the biological active molecule, cells containing and expressing these nucleic acids, as well as methods and apparatuses involving above products, inso far as related to the biologically active protein being to cAMP dependent protein kinases.

4. Claims: Partially: 1-43, 46, 59-82 and 88; Entirely: 52

MMethods for extracting information from influences on a living cell involving observing spatial redistribution or modulation of a luminophore linked to a biologically active

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

molecule, in particular to a molecule involved in intracellular signalling pathways, nucleic acids encoding fusion proteins comprising bothe the luminophore and the biological active molecule, cells containing and expressing these nucleic acids, as well as methods and apparatuses involving above products, inso far as related to the biologically active protein being cGMP dependent protein kinases

5. Claims: Partially: 1-43, 59-82 and 88; Entirely: 58

Methods for extracting information from influences on a living cell involving observing spatial redistribution or modulation of a luminophore linked to a biologically active molecule, in particular to a molecule involved in intracellular signalling pathways, nucleic acids encoding fusion proteins comprising bothe the luminophore and the biological active molecule, cells containing and expressing these nucleic acids, as well as methods and apparatuses involving above products, inso far as related to the biologically active protein being protein phosphatases

6. Claims: Partially: 1-41, 43, 59-82 and 88; Entirely: 44

Methods for extracting information from influences on a living cell involving observing spatial redistribution or modulation of a luminophore linked to a biologically active molecule, in particular to a molecule involved in intracellular signalling pathways, nucleic acids encoding fusion proteins comprising bothe the luminophore and the biological active molecule, cells containing and expressing these nucleic acids, as well as methods and apparatuses involving above products, inso far as related to the biologically active protein being to transcription factors

7. Claims: Partially: 1-41, 43, 59-82 and 88; Entirely: 45

Methods for extracting information from influences on a living cell involving observing spatial redistribution or modulation of a luminophore linked to a biologically active molecule, in particular to a molecule involved in intracellular signalling pathways, nucleic acids encoding fusion proteins comprising bothe the luminophore and the biological active molecule, cells containing and expressing these nucleic acids, as well as methods and apparatuses involving above products, inso far as related to the biologically active protein being to proteins associated with the cytoskeletal network

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INTERNATIONAL SEARCH REPORT

Information on patent family members

In..ational Application No
PCT/DK 98/00145

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9711094 A	27-03-1997	AU 4482996 A	09-04-1997
		CA 2232727 A	27-03-1997
		EP 0851874 A	08-07-1998
WO 9101305 A	07-02-1991	AU 6054590 A	22-02-1991
		CA 2064766 A	23-01-1991
		EP 0484369 A	13-05-1992
		JP 5501862 T	08-04-1993
		US 5683888 A	04-11-1997
WO 9507463 A	16-03-1995	US 5491084 A	13-02-1996
		AU 694745 B	30-07-1998
		AU 7795794 A	27-03-1995
		CA 2169298 A	16-03-1995
		EP 0759170 A	26-02-1997
		JP 9505981 T	17-06-1997
WO 9623898 A	08-08-1996	AU 4483096 A	21-08-1996
		CA 2217700 A	08-08-1996
		EP 0815257 A	07-01-1998
WO 9603649 A	08-02-1996	AU 3146095 A	22-02-1996
		CA 2195629 A	08-02-1996
		EP 0772773 A	14-05-1997
		JP 10503369 T	31-03-1998
WO 9720931 A	12-06-1997	AU 1283497 A	27-06-1997
		CA 2239951 A	12-06-1997
WO 9730074 A	21-08-1997	AU 2272397 A	02-09-1997
WO 9802571 A	22-01-1998	AU 3801997 A	09-02-1998
WO 9830715 A	16-07-1998	AU 5090498 A	03-08-1998
WO 9423039 A	13-10-1994	AU 677834 B	08-05-1997
		AU 6382394 A	24-10-1994
		EP 0703984 A	03-04-1996
		JP 9501302 T	10-02-1997
		AU 696939 B	24-09-1998
		AU 1586195 A	29-08-1995
		CA 2182967 A	17-08-1995
		EP 0742827 A	20-11-1996
		WO 9521923 A	17-08-1995
		JP 9508795 T	09-09-1997

BNSDOCID: <WO___9845704A3_I_>

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